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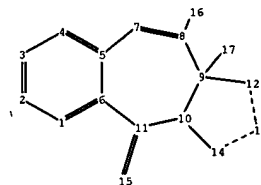
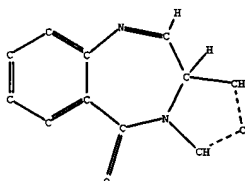
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L8



chain nodes :

15 16 17

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14

chain bonds :

8-16 9-17 11-15

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-11 7-8 8-9 9-10 9-12 10-11  
10-14 12-13 13-14

exact/norm bonds :

5-7 6-11 7-8 8-9 9-10 9-12 10-11 10-14 11-15 12-13 13-14

exact bonds :

8-16 9-17

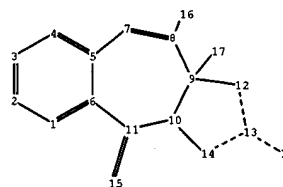
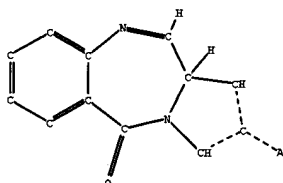
normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom  
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS

214



chain nodes :

15 16 17 18

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14

chain bonds :

8-16 9-17 11-15 13-18

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-11 7-8 8-9 9-10 9-12 10-11  
10-14 12-13 13-14

exact/norm bonds :

5-7 6-11 7-8 8-9 9-10 9-12 10-11 10-14 11-15 12-13 13-14 13-18

exact bonds :

8-16 9-17

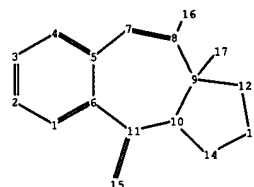
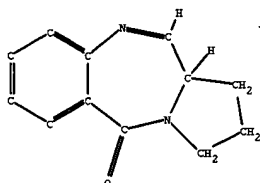
normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom  
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS  
18:CLASS

L13



chain nodes :

15 16 17

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14

chain bonds :

8-16 9-17 11-15

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-11 7-8 8-9 9-10 9-12 10-11  
10-14 12-13 13-14

exact/norm bonds :

5-7 6-11 7-8 8-9 9-10 9-12 10-11 10-14 11-15 12-13 13-14

exact bonds :

8-16 9-17

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom  
10:Atom 11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS

09/763,767

=> D HIS

(FILE 'HOME' ENTERED AT 18:03:05 ON 28 SEP 2001)

FILE 'REGISTRY' ENTERED AT 18:03:09 ON 28 SEP 2001

FILE 'STNGUIDE' ENTERED AT 18:05:04 ON 28 SEP 2001

FILE 'REGISTRY' ENTERED AT 18:05:47 ON 28 SEP 2001

L7               STRUCTURE UPLOADED  
L8               QUE L7  
L9               12 S L8  
L10              250 S L8 SSS FUL

FILE 'CAPLUS' ENTERED AT 18:08:53 ON 28 SEP 2001

L11             145 S L10

FILE 'STNGUIDE' ENTERED AT 18:09:10 ON 28 SEP 2001

FILE 'REGISTRY' ENTERED AT 18:10:18 ON 28 SEP 2001

L12             STRUCTURE UPLOADED  
L13             QUE L12  
L14             STRUCTURE UPLOADED  
L15             QUE L14  
L16             10 S L13   SUB=L10 SAM  
L17             2 S L14   SUB=L10 SAM  
L18             172 S L13   SUB=L10 FUL  
L19             54 S L14   SUB=L10 FUL

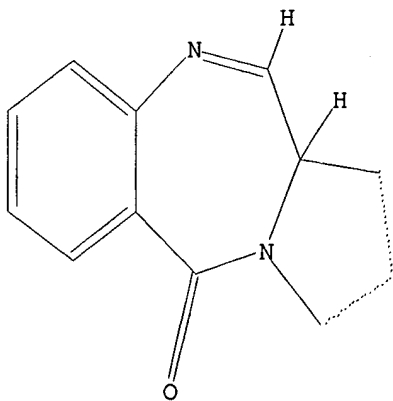
FILE 'CAPLUS' ENTERED AT 18:15:31 ON 28 SEP 2001

L20             86 S L18  
L21             50 S L19  
L22             122 S L20 OR L21  
L23             88 S L22 AND JOURNAL/DT  
L24             4 S L23 AND 2001/SO  
L25             11 S L23 AND 2000/SO  
L26             107 S L22 NOT (L24 OR L25)

=> d 18

L8 HAS NO ANSWERS

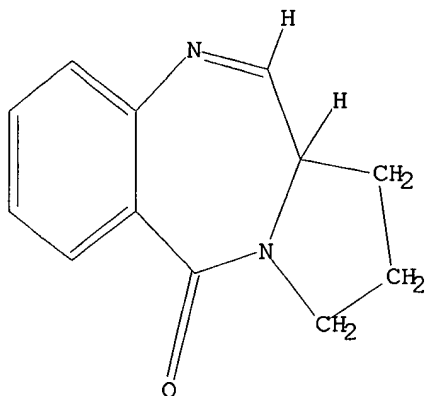
L7               STR



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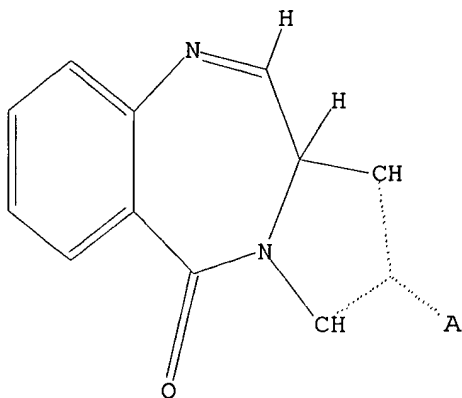
Structure attributes must be viewed using STN Express query preparation.  
L8 QUE ABB=ON PLU=ON L7

=> d 113  
L13 HAS NO ANSWERS  
L12 STR



Structure attributes must be viewed using STN Express query preparation.  
L13 QUE ABB=ON PLU=ON L12

=> d 114  
L14 HAS NO ANSWERS  
L14 STR



Structure attributes must be viewed using STN Express query preparation.

=> d bib abs hitstr 126 1-107

09/763,767

L26 ANSWER 1 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 2000:161285 CAPLUS  
DN 132:207852  
TI Solid-phase preparation and combinatorial libraries of  
pyrrolobenzodiazepine derivatives for drug screening  
IN Thurston, David Edwin; Howard, Philip Wilson  
PA The University of Portsmouth Higher Education Corporation, UK  
SO PCT Int. Appl., 65 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012509	A2	20000309	WO 1999-GB2839	19990827
	WO 2000012509	A3	20000706		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9955262	A1	20000321	AU 1999-55262	19990827
	EP 1107970	A2	20010620	EP 1999-941767	19990827
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
PRAI	GB 1998-18732	A	19980827		
	WO 1999-GB2839	W	19990827		
OS	MARPAT 132:207852				
GI					

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I are prepd. [wherein: R = (un)substituted alk(en/yn)yl, aralkyl, aryl, or heteroat. analogs; R2 and R3 = H, R, OH, OR, O, :CHR, :CH2, CH2CO2R, CH2CO2H, CH2SO2R, OSO2R, CO2R, COR, and cyano; optionally double bond in ring; R6, R7, R8, and R9 = H, R, OH, OR, halo, NO2, amino, Me3Sn; or R7R8 = O(CH2)1-20; R11 = H or R; Q = S, O, or NH; L = linking group or bond; Sup = solid support; or where 1 or more of R2, R3, R6, R7 and R8 = independently = H-(T)n-X-Y-A- where: X = CO, NH, S or O; T = combinatorial unit; Y = divalent group such that HY = R; A = O, S, NH, or bond; and n = pos. integer]. The compds. are intermediates for pyrrolobenzodiazepine derivs. II, which are claimed as being potentially useful for treatment of bacterial, parasitic, viral, and gene-based diseases. For example, the supported chloroformate ester III underwent (1) elaboration with 4,5-dimethoxyanthranilic acid, (2) amidation with 2-pyrrolidinemethanol, and (3) oxidative cyclization using SO3.pyridine and DMSO, to give the invention compd. IV. Photochem. cleavage of IV gave the corresponding aminal, which was dehydrated in situ to give the corresponding compd. V. The cleavage product showed cytotoxicity against human leukemia cells which was identical to that of authentic samples of V. Another compd. I was derivatized at a sidechain using 3 amino acids in

3 chain positions to give a 27-member combinatorial library.

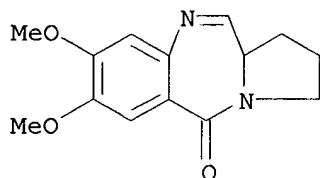
IT **260417-09-2P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compd.; solid-phase prepn. and combinatorial libraries of pyrrolobenzodiazepine derivs. for drug screening)

RN 260417-09-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-dimethoxy- (9CI) (CA INDEX NAME)



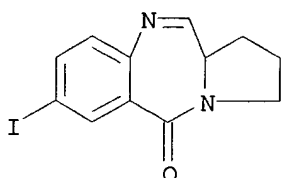
IT **260417-05-8P 260417-31-0P 260417-36-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(target compd.; solid-phase prepn. and combinatorial libraries of pyrrolobenzodiazepine derivs. for drug screening)

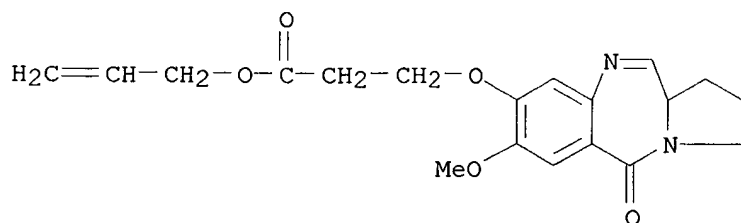
RN 260417-05-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-iodo- (9CI) (CA INDEX NAME)



RN 260417-31-0 CAPLUS

CN Propanoic acid, 3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]-, 2-propenyl ester (9CI) (CA INDEX NAME)



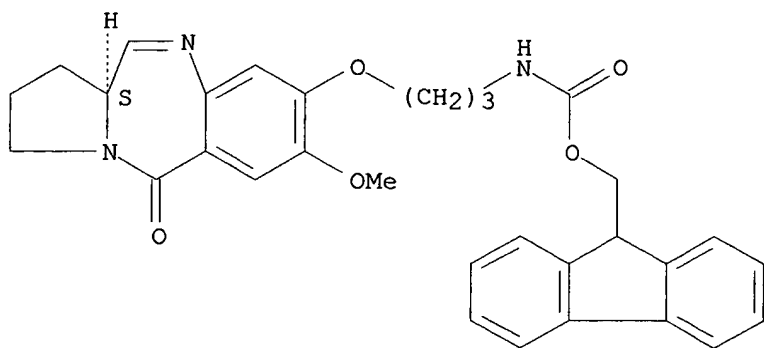
RN 260417-36-5 CAPLUS

CN Carbamic acid, [3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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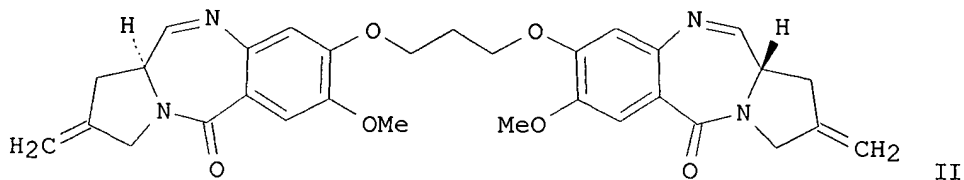
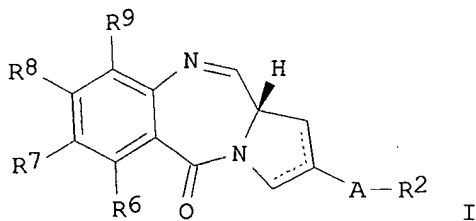


09/763,767

applicants

L26 ANSWER 2 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 2000:161284 CAPLUS  
DN 132:207851  
TI Preparation of pyrrolobenzodiazepines (PBDs) as antitumor agents  
IN Thurston, David Edwin; Howard, Philip Wilson  
PA The University of Portsmouth Higher Education Corporation, UK  
SO PCT Int. Appl., 258 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012508	A2	20000309	WO 1999-GB2838	19990827
	WO 2000012508	A3	20000921		
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	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9956351	A1	20000321	AU 1999-56351	19990827
	EP 1109812	A2	20010627	EP 1999-943066	19990827
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
PRAI	GB 1998-18733	A	19980827		
	GB 1999-1929	A	19990128		
	WO 1999-GB2838	W	19990827		
OS	MARPAT 132:207851				
GI					



AB 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one derivs. (I) [wherein A = CH<sub>2</sub> or a single bond; R = (un)substituted (ar)alkyl, (ar)alkenyl, or (ar)alkynyl;

R2 = R, OH, OR, CO2H, CO2R, COH, COR, SO2R, CN; R6, R7, R8, and R9 = independently H, R, OH, OR, halo, NH2, NHR, NO2, SnMe3; or the compd. is a dimer with each monomer being the same or different and being of formula I and the R8 groups of the monomers form a -X-R'-X- bridge, where R' is an alkylene chain which may contain .gtoreq. 1 heteroatoms and/or arom. rings and/or carbon-carbon double or triple bonds, and each X = independently O, S, or N] were prepd. for the treatment of gene-based diseases, e.g. neoplastic diseases and Alzheimer's disease, and also bacterial, parasitic, and viral infections. For example, II was synthesized in a 6-step sequence. 1',3'-Bis(4-carboxy-2-methoxy-5-nitrophenoxy)propane (prepn. given) was bisamidated with (2S)-2-(tert-butyltrimethylsilyloxymethyl)-4-methylenepyrrolidine (74%). TBAF-mediated cleavage of the silyl protecting groups (94%), followed by redn. of the nitro groups by NH2NH2 in the presence of Raney Ni (63%) and N-acylation with allyl chloroformate (50%), gave the protected diamine. Ring closure was accomplished under Swern oxidn. conditions, (COCl)2-DMSO and TEA, (32%). Finally, the imine was formed from the carbinolamine by N-deprotection using Pd(PPh3)4 and elimination of H2O (77%). Both large scale in vitro cytotoxicity cell screens and in vivo hollow fiber and human tumor xenograft assays were performed on selected compds. of the invention. For instance, II exhibited potent and selective cytotoxicity against the lung cancer cell line NCI-H460, the colon cell line HCC-2998, the CNS cancer cell line SNB-75, and the melanoma cell lines MALME-3M (very potent, 0.08 .mu.M) and UACC-62 (very potent, 0.07 .mu.M). In human xenograft studies against five types of tumors, II demonstrated anticancer activity with mixed toxicity results. In addn., II was shown to be the most potent DNA-stabilizing agent known to date according to a DNA helix melting temp. assay. The IC50 value for II in the A2780 human ovarian carcinoma cell line was only 23 pM, a 320-fold increase in cytotoxicity compared to the known antitumor agent DSB-120 (IC50 = 5.2 nM). Remarkably, II was also almost 9000-fold more potent in the cisplatin-resistant A2780cisR cell line (IC50 = 24 pM) than DSB-120 (IC50 = 0.21 mM), suggesting that II may have potential in the treatment of cisplatin-refractory disease.

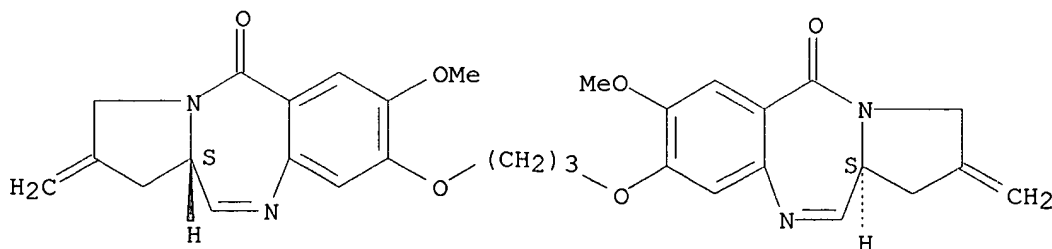
IT 232931-57-6P, SJG 136

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(target compd.; prepn. of 5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one antitumor agents from 2-amino- or 2-nitrobenzoic acid derivs. and pyrrolidines)

RN 232931-57-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-2-methylene-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



IT 110715-89-4P, AG 140 133954-34-4P, DRH 271  
 187083-51-8P, AG 105 215723-10-7P, UP 2026  
 219537-19-6P, AG 135 260417-36-5P, UP 2088  
 260417-62-7P 260417-63-8P 260417-64-9P  
 260543-36-0P, SB-A 67 260543-52-0P, SJG 245  
 260543-54-2P, SJG 301 260543-56-4P, SJG 303  
 260543-57-5P, AN-SJG 260543-81-5P, KEC 570  
 260544-27-2P, UP 2089 260546-05-2P, BSD-SJG  
 260546-06-3P, SJG 244 260546-07-4P, MMY-SJG  
 260546-08-5P, UP 2067 260546-09-6P, DRH 165  
 260546-54-1P, DRH-NA 7 260546-58-5P, DRH 69  
 260546-76-7P, DRH 168 260546-91-6P, AG 150  
 260546-93-8P, DRH 105 260546-94-9P, UP 2028  
 260546-96-1P, UP 2005 260546-97-2P, UP 2006  
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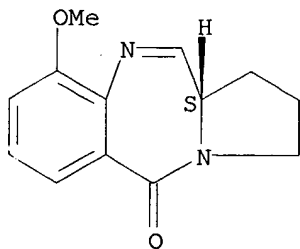
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compd.; prepn. of 5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one antitumor agents from 2-amino- or 2-nitrobenzoic acid derivs. and pyrrolidines)

RN 110715-89-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

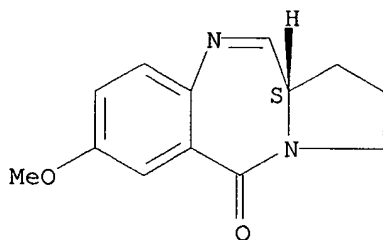
Absolute stereochemistry.



RN 133954-34-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



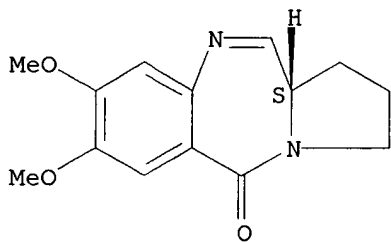
RN 187083-51-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-

09/763,767

dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

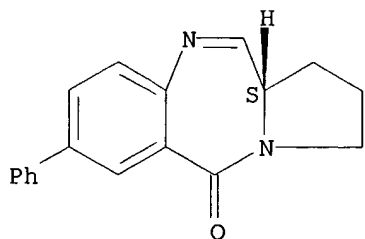
Absolute stereochemistry.



RN 215723-10-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-phenyl-,  
(11aS)- (9CI) (CA INDEX NAME)

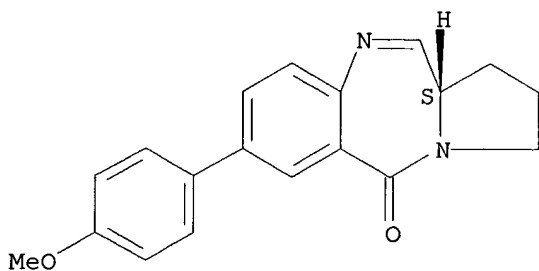
Absolute stereochemistry.



RN 219537-19-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(4-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

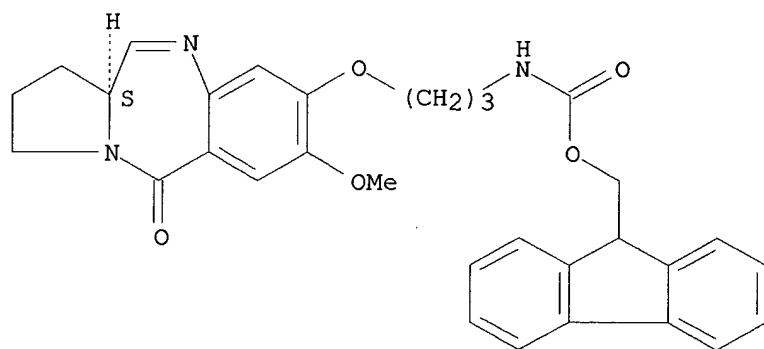


RN 260417-36-5 CAPLUS

CN Carbamic acid, [3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]-, 9H-fluoren-9-ylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

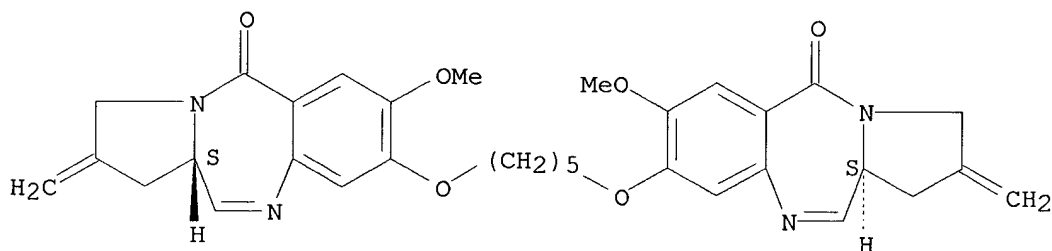
09/763,767



RN 260417-62-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanediy]bis(oxy)bis[1,2,3,11a-tetrahydro-7-methoxy-2-methylene-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

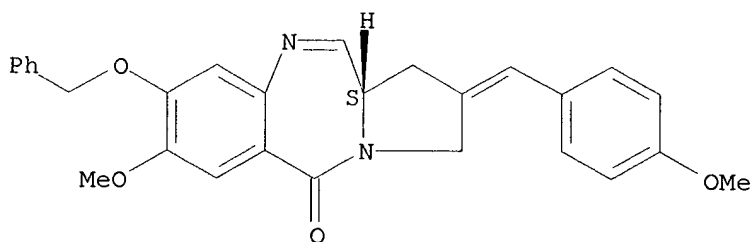


RN 260417-63-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-2-[(4-methoxyphenyl)methylene]-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

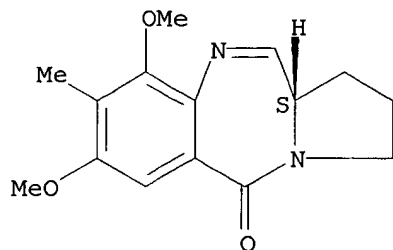


RN 260417-64-9 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,9-dimethoxy-8-methyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

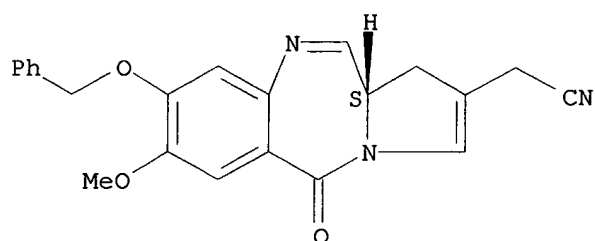
09/763,767



RN 260543-36-0 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acetonitrile, 5,11a-dihydro-7-methoxy-5-oxo-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

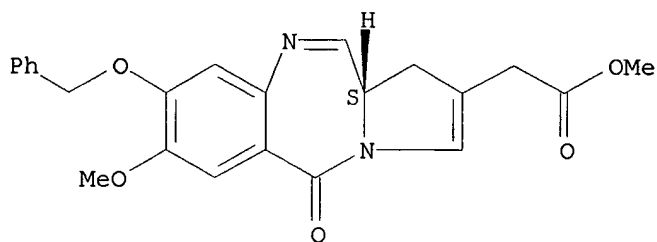
Absolute stereochemistry.



RN 260543-52-0 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acetic acid, 5,11a-dihydro-7-methoxy-5-oxo-8-(phenylmethoxy)-, methyl ester, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

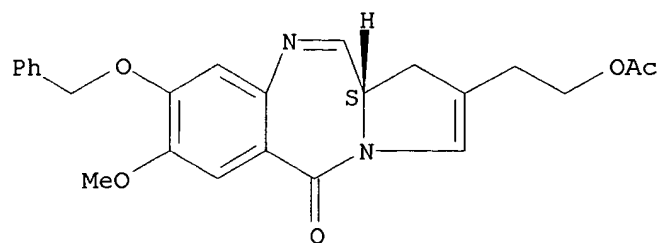


RN 260543-54-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-[2-(acetyloxy)ethyl]-1,11a-dihydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

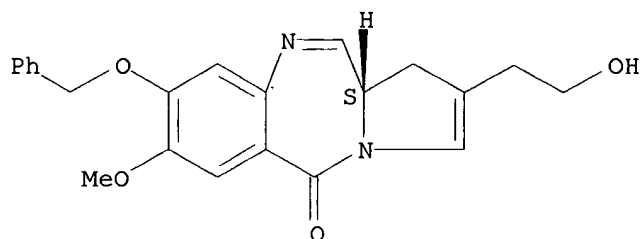
Absolute stereochemistry. Rotation (+).

09/763,767



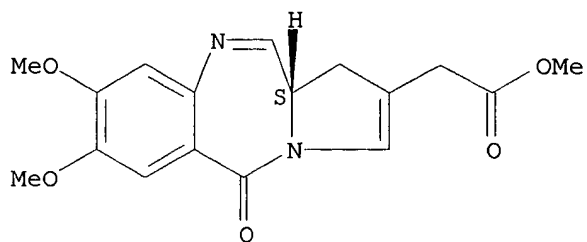
RN 260543-56-4 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,11a-dihydro-2-(2-hydroxyethyl)-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 260543-57-5 CAPLUS  
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acetic acid, 5,11a-dihydro-7,8-dimethoxy-5-oxo-, methyl ester, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

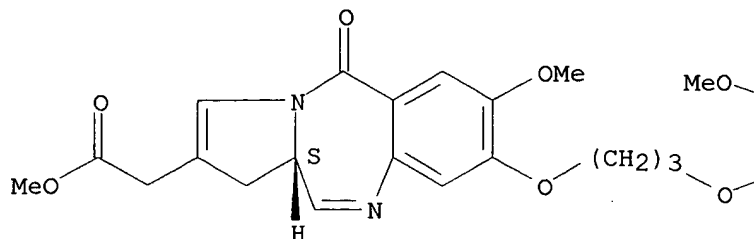


RN 260543-81-5 CAPLUS  
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acetic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[5,11a-dihydro-7-methoxy-5-oxo-, dimethyl ester, (11aS,11'aS)- (9CI) (CA INDEX NAME)

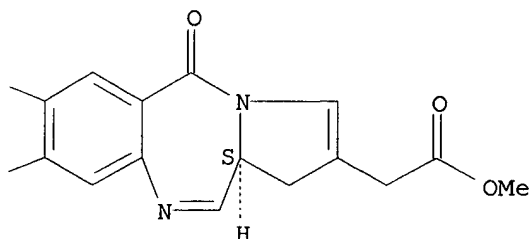
Absolute stereochemistry.



PAGE 1-A



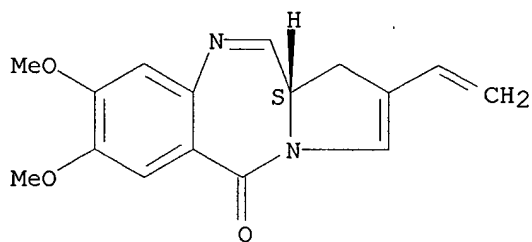
PAGE 1-B



RN 260544-27-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethenyl-1,11a-dihydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

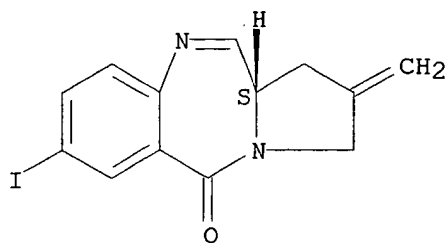
Absolute stereochemistry.



RN 260546-05-2 CAPLUS

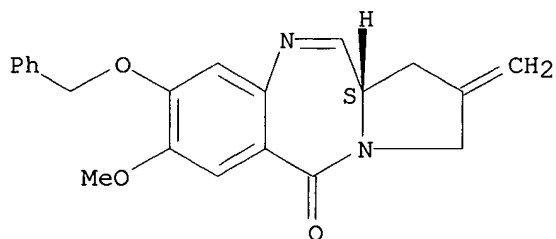
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-iodo-2-methylene-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



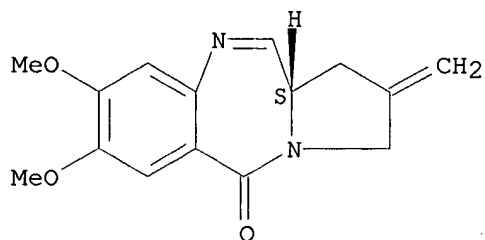
RN 260546-06-3 CAPLUS  
 CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-2-methylene-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 260546-07-4 CAPLUS  
 CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-dimethoxy-2-methylene-, (11aS)- (9CI) (CA INDEX NAME)

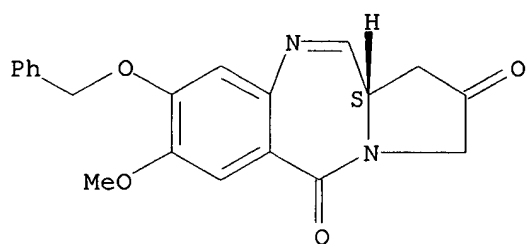
Absolute stereochemistry.



RN 260546-08-5 CAPLUS  
 CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H)-dione, 1,11a-dihydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

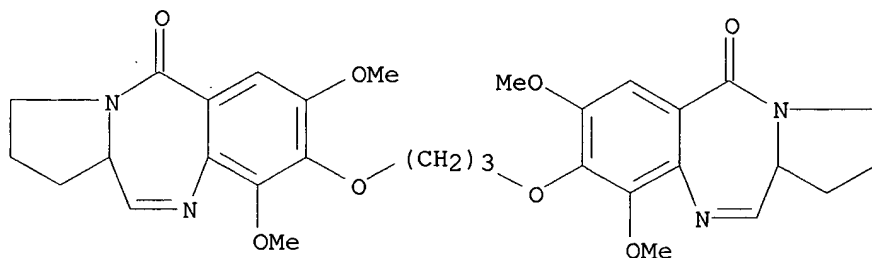
09/763,767



RN 260546-09-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7,9-dimethoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

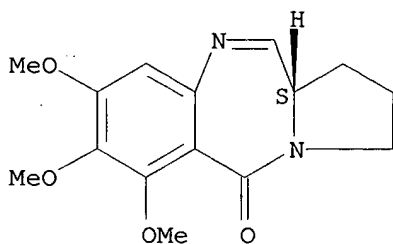
Absolute stereochemistry.



RN 260546-54-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-6,7,8-trimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

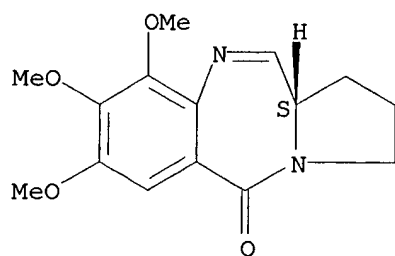


RN 260546-58-5 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8,9-trimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

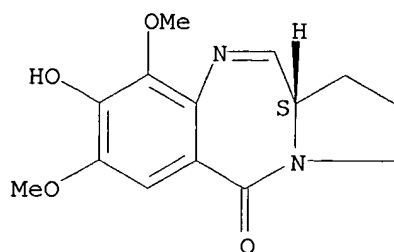
09/763,767



RN 260546-76-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7,9-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

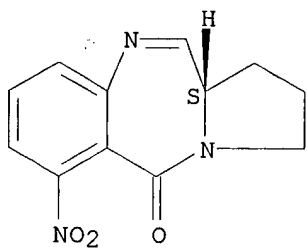
Absolute stereochemistry.



RN 260546-91-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-6-nitro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

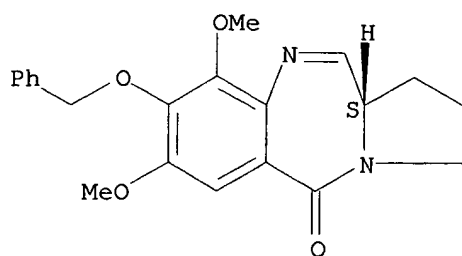


RN 260546-93-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,9-dimethoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

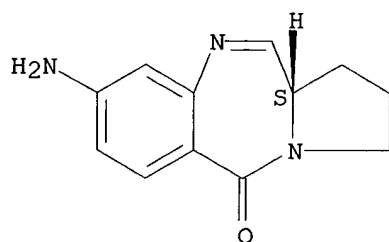
09/763,767



RN 260546-94-9 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8-amino-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

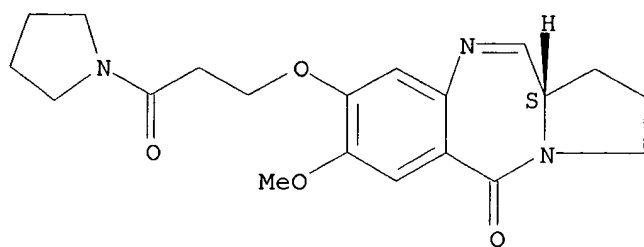
Absolute stereochemistry.



RN 260546-96-1 CAPLUS

CN Pyrrolidine, 1-[1-oxo-3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

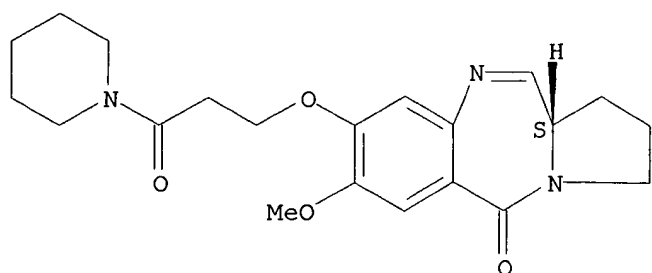


RN 260546-97-2 CAPLUS

CN Piperidine, 1-[1-oxo-3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

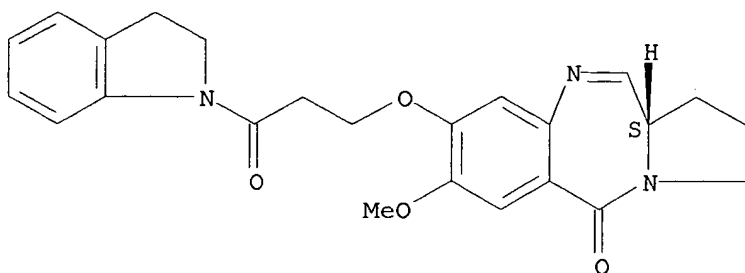
09/763,767



RN 260546-99-4 CAPLUS

CN 1H-Indole, 2,3-dihydro-1-[1-oxo-3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

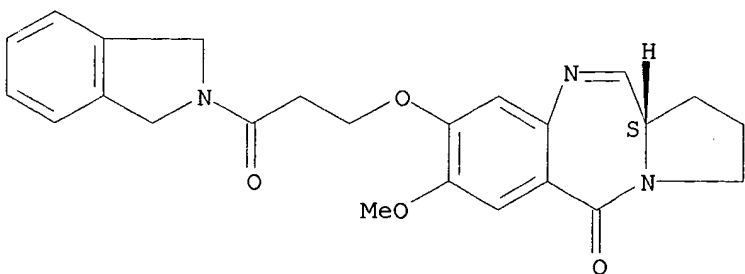
Absolute stereochemistry.



RN 260547-00-0 CAPLUS

CN 1H-Isoindole, 2,3-dihydro-2-[1-oxo-3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

126 ANSWER 3 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 2000:161283 CAPLUS

DN 132:207703

TI Preparation of pyrrolobenzodiazepines (PBDs) as antitumor antibiotics

IN Thurston, David Edwin; Howard, Philip Wilson

PA The University of Portsmouth Higher Education Corporation, UK

SO PCT Int. Appl., 101 pp.

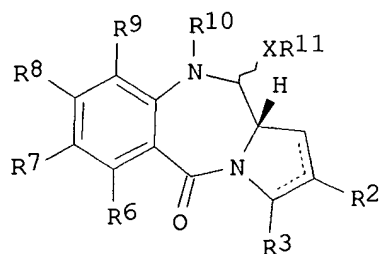
CODEN: PIXXD2

DT Patent

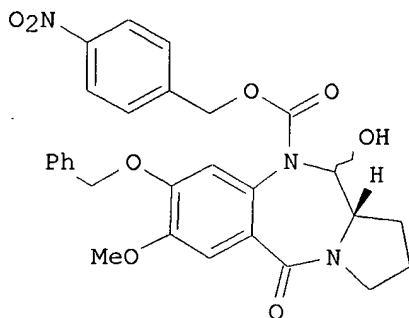
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012507	A2	20000309	WO 1999-GB2837	19990827
	WO 2000012507	A3	20000831		
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9955261	A1	20000321	AU 1999-55261	19990827
	EP 1109811	A2	20010627	EP 1999-941766	19990827
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
PRAI	GB 1998-18731	A	19980827		
	WO 1999-GB2837	W	19990827		
OS	MARPAT 132:207703				
GI					



I



II

AB 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one derivs. (I) [wherein R = (un)substituted (ar)alkyl, etc.; R2 and R3 = independently H, R, OH, OR, =O, =CH-R, =CH2, CH2-CO2R, CH2-CO2H, CH2-SO2R, O-SO2-R, CO2R, COR, or CN; R6, R7, R8, and R9 = independently H, R, OH, OR, halo, NH2, NO2, or Me3Sn; or R7 and R8 together form a -O-(CH2)p-O- group, where p = 1 or 2; or the compd. is a dimer with each monomer being the same or different and being of formula I and the R8 groups of the monomers form a -T-R'-T- bridge, where R' is an alkylene chain which may contain .gtoreq. 1 heteroatoms

and/or arom. rings and/or carbon-carbon double or triple bonds, and each T = independently O, S, or N; R10 = a therapeutically removable N-protecting group; R11 = H or R; X is S, O, or NH] were prepd. for the treatment of cancer and other site-specific diseases where a local increase of toxicity is beneficial to the patient. Examples include the syntheses of benzyl DC-81, benzyl tomaymycin, and DSB-120 prodrugs starting from 2-nitrobenzoic acid derivs. and pyrrolidines. Data from enzyme and light activation studies and cytotoxicity assays are also given. For example, the nitroreductase-activated benzyl DC-81 (II) was formed in a 6-step sequence involving: (1) benzylation of vanillic acid (67%); (2) ring nitration (82%); (3) amidation with (2S)-pyrrolidinemethanol (88%); (4) redn. of the nitro group (81%); (5) N-addn. of 4-nitrobenzyl chloroformate; and (6) cyclization using Swern oxidn. conditions (31%). In the presence of nitroreductase and the NADH co-factor, II demonstrated antitumor activity (IC50 = 1-5 .mu.M) against the SW1116 and LS174T human adenocarcinoma colonic cell lines. II proved non-toxic in SW1116 cells at concns. .ltoreq. 500 .mu.M and showed slight toxicity in LS174T cells at concns. > 100 .mu.M. I may also be suitable for treating bacterial, parasitic, or viral infections by exploiting a unique enzyme produced at the site of infection which is not natural to the host, or by exploiting an elevation in the amt. of an enzyme which does occur naturally in the host.

IT 127810-79-1, Benzyl DC 81 140676-21-7, DSB 120

187083-51-8, UP 2025

RL: BAC (Biological activity or effector, except adverse); THU

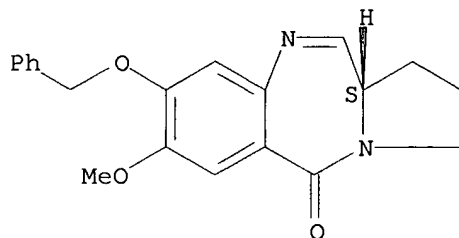
(Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of pyrrolobenzodiazepinone prodrugs from 2-nitrobenzoic acid derivs. and pyrrolidines for the treatment of cancer)

RN 127810-79-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



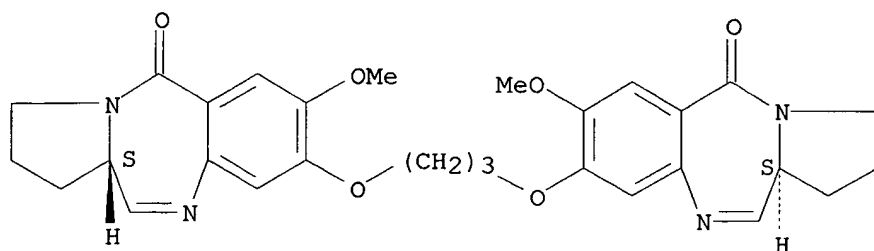
RN 140676-21-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



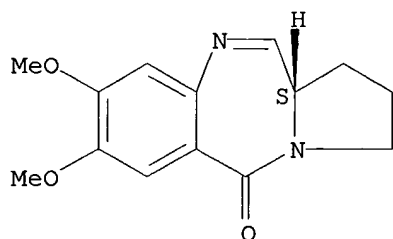
09/763,767



RN 187083-51-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

126 ANSWER 4 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 2000:161282 CAPLUS  
DN 132:208134

TI Preparation of peptidyl pyrrolobenzodiazepines as pharmaceuticals  
IN Thurston, David Edwin; Howard, Philip Wilson  
PA The University of Portsmouth Higher Education Corporation, UK  
SO PCT Int. Appl., 158 pp.  
CODEN: PIXXD2

DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000012506	A2	20000309	WO 1999-GB2836	19990827
	WO 2000012506	A3	20000629		
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	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9955260	A1	20000321	AU 1999-55260	19990827
	EP 1107969	A2	20010620	EP 1999-941765	19990827
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
PRAI	GB 1998-18730	A	19980827		
	WO 1999-GB2836	W	19990827		
OS	MARPAT 132:208134				
GI					

no  
adp

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Benzodiazepines I [X = CO<sub>2</sub>H, NH<sub>2</sub> or protected amino, SH, OH; A = O, S, NH, or a single bond; R<sub>2</sub>, R<sub>3</sub> = H, R, OH, OR, :O, :CHR, :CH<sub>2</sub>, CH<sub>2</sub>CO<sub>2</sub>R, CH<sub>2</sub>CO<sub>2</sub>H, CH<sub>2</sub>SO<sub>2</sub>R, OSO<sub>2</sub>R, CO<sub>2</sub>R, COR, CN, where R = alkyl, alkenyl, alkynyl, aralkyl, (un)substituted aryl; there is optionally a double bond between C<sub>1</sub> and C<sub>2</sub> or C<sub>2</sub> and C<sub>3</sub>; R<sub>6</sub>, R<sub>7</sub>, R<sub>9</sub> = H, R, OH, OR, halo, nitro, amino, Me<sub>3</sub>Sn; R<sub>11</sub> = H or R; Q = S, O or NH; R<sub>10</sub> is a nitrogen-protecting group; Y is a divalent group such that HY = R] were prepd. and incorporated into peptides for use as pharmaceuticals. Thus, pyrrolo[2,1-c][1,4]benzodiazepine deriv. II (Fmoc = fluorenylmethoxycarbonyl) was prepd. and applied to the synthesis of a 27-member glycine/valine/phenylalanine tripeptide library which was screened for inhibition of leukemia cells.

IT 260449-68-1P 260449-69-2P 260449-70-5P  
260449-71-6P 260449-72-7P 260449-73-8P  
260449-74-9P 260449-75-0P 260449-76-1P  
260449-77-2P 260449-78-3P 260449-79-4P  
260449-80-7P 260449-81-8P 260449-82-9P  
260449-83-0P 260449-84-1P 260449-85-2P  
260449-86-3P 260449-88-5P 260449-90-9P  
260449-92-1P 260449-94-3P 260449-96-5P

260449-98-7P 260450-00-8P 260450-02-0P  
 260450-04-2P 260450-06-4P 260450-08-6P  
 260450-10-0P 260450-12-2P 260450-14-4P  
 260450-16-6P 260450-18-8P 260450-20-2P  
 260450-22-4P 260450-24-6P 260450-26-8P  
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 260450-40-6P 260450-41-7P 260450-43-9P  
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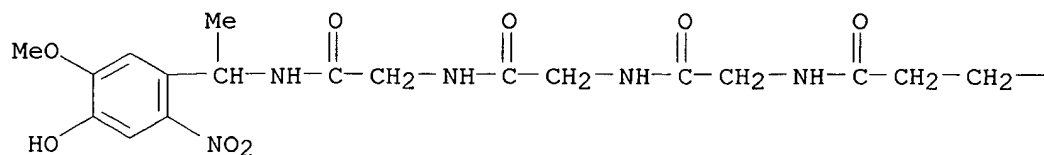
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptidyl pyrrolobenzodiazepines as pharmaceuticals)

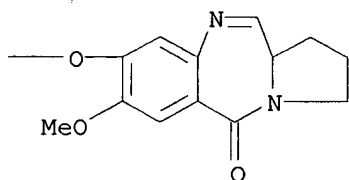
RN 260449-68-1 CAPLUS

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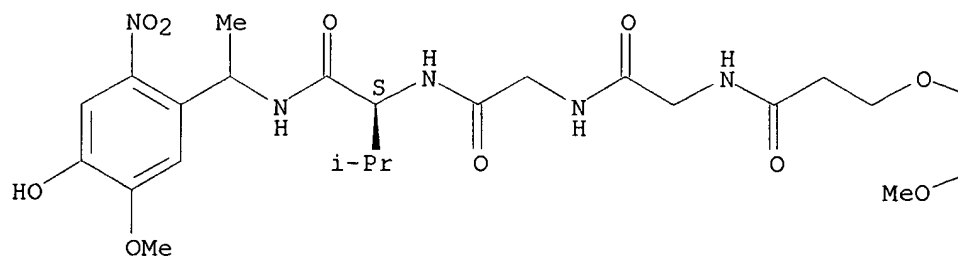


RN 260449-69-2 CAPLUS

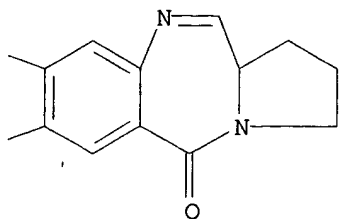
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Absolute stereochemistry.

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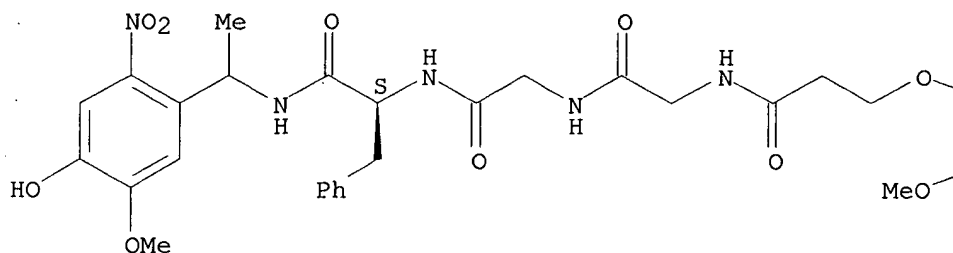


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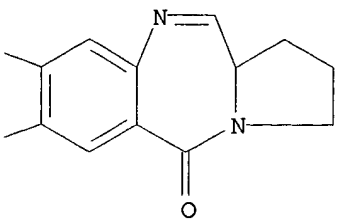
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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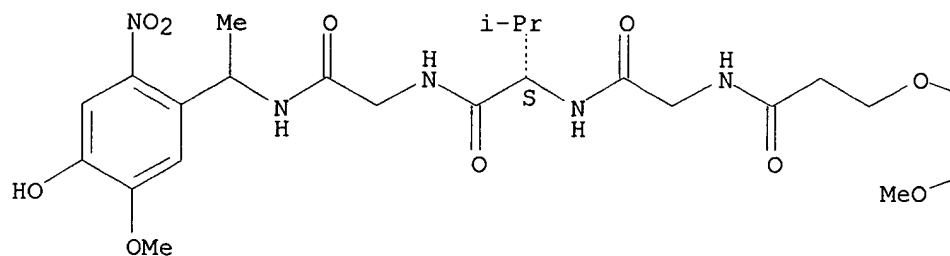


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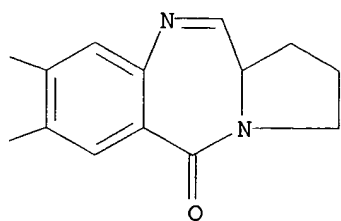
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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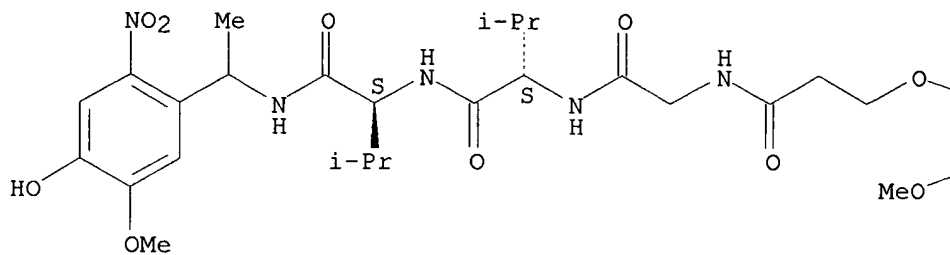


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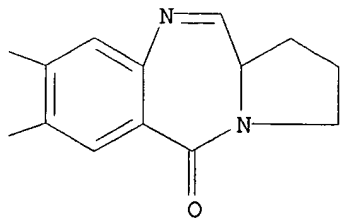
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Absolute stereochemistry.

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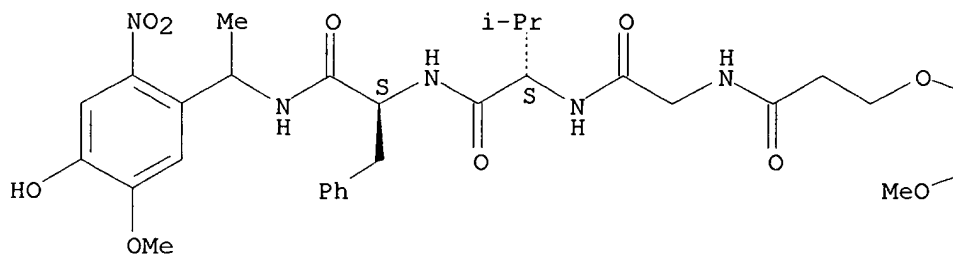
09/763,767

RN 260449-73-8 CAPLUS

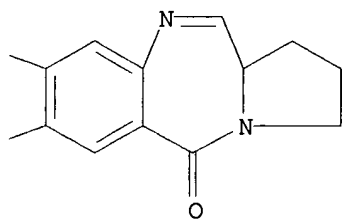
CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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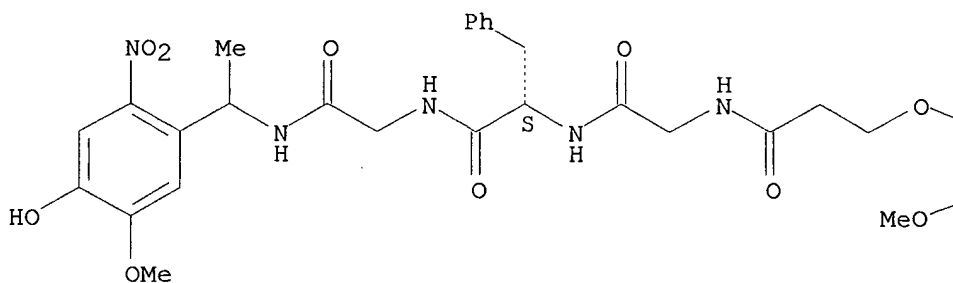


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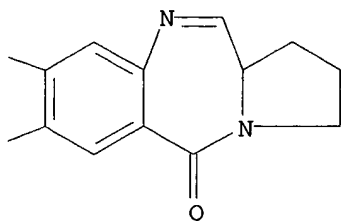
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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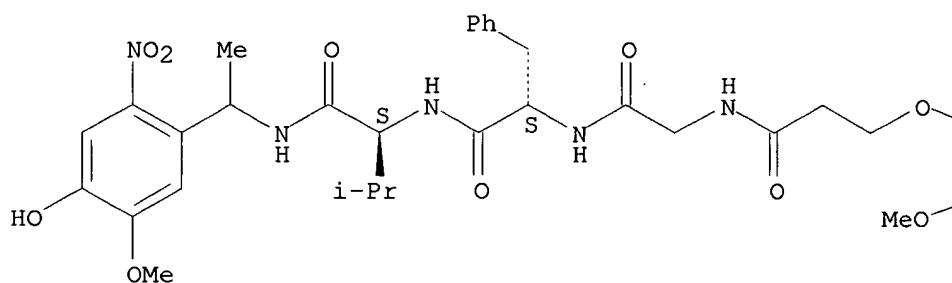


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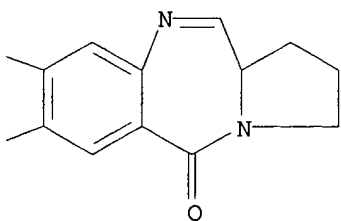
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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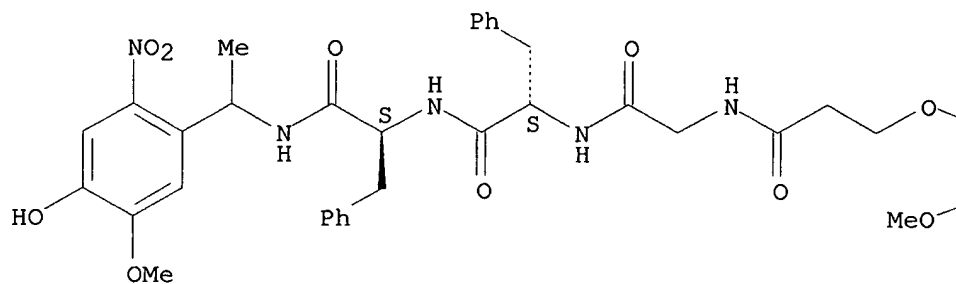


RN 260449-76-1 CAPLUS

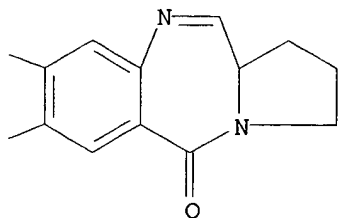
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Absolute stereochemistry.

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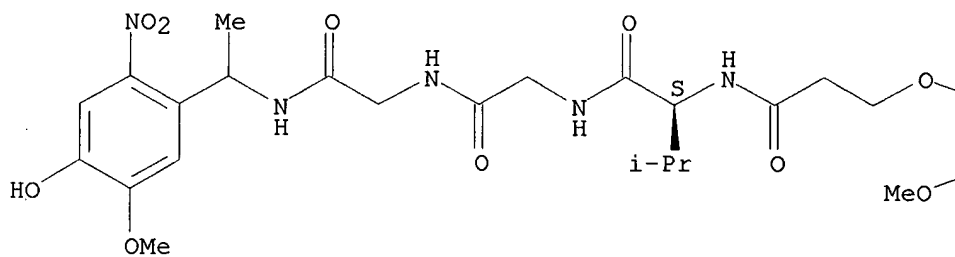


RN 260449-77-2 CAPLUS

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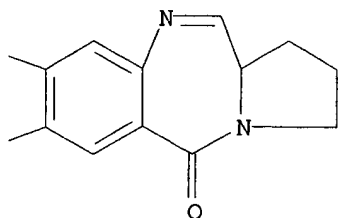
Absolute stereochemistry.

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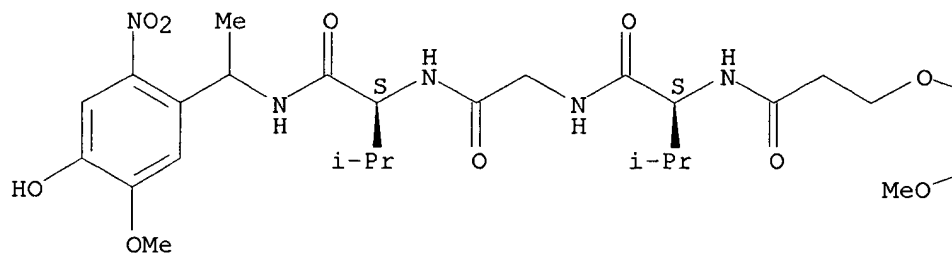


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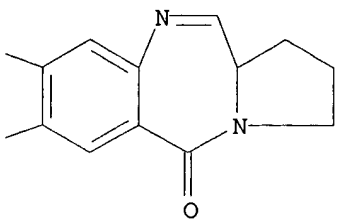
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Absolute stereochemistry.

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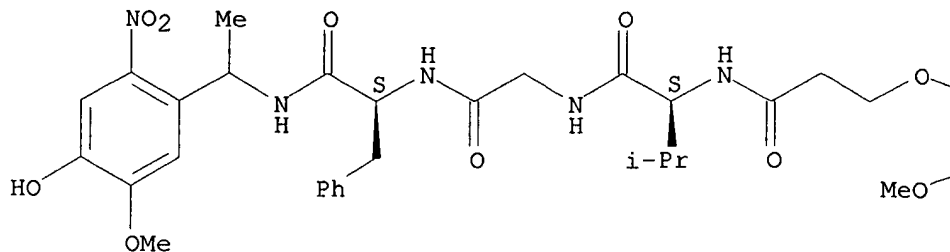


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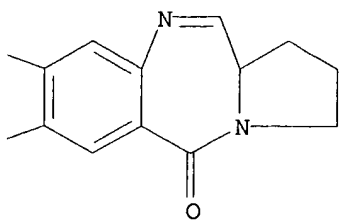
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Absolute stereochemistry.

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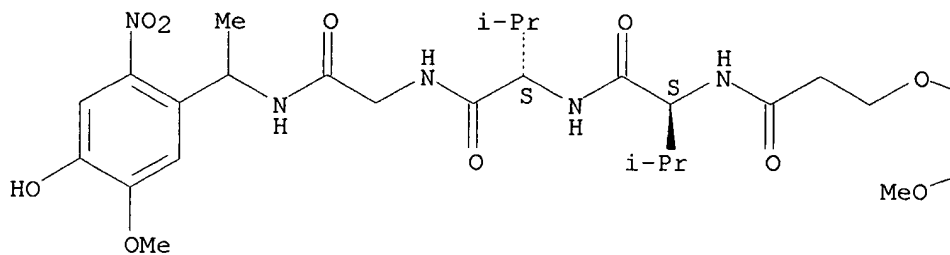


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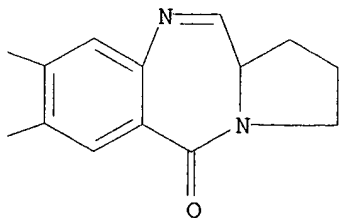
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Absolute stereochemistry.

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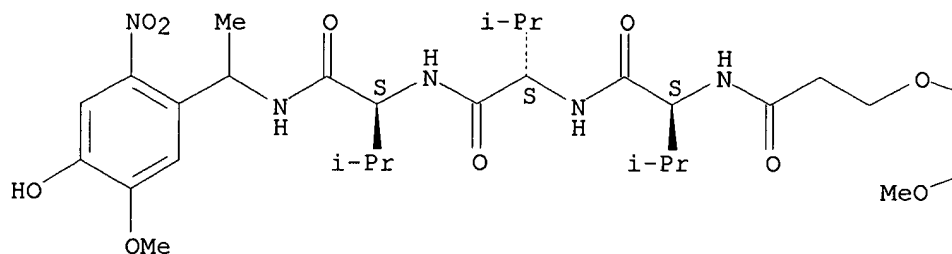
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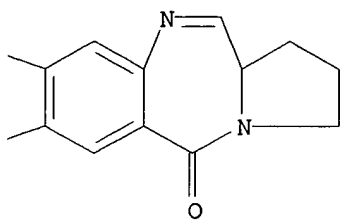
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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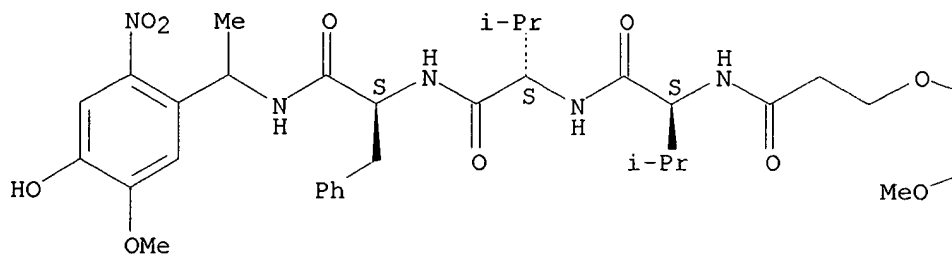


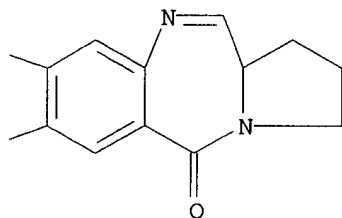
RN 260449-82-9 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-valyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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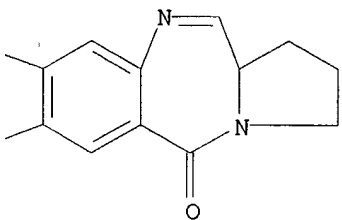
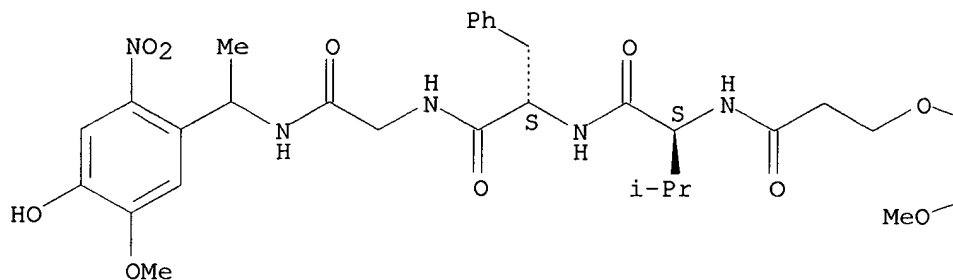




RN 260449-83-0 CAPLUS

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Absolute stereochemistry.

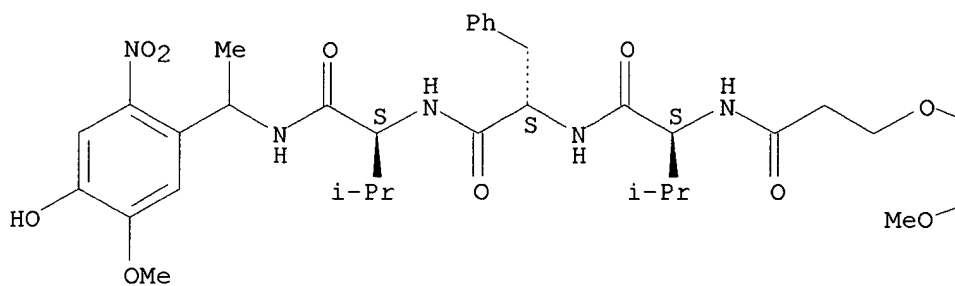


RN 260449-84-1 CAPLUS

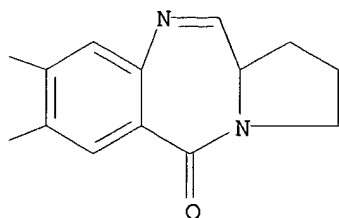
CN L-Valinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-valyl-L-phenylalanyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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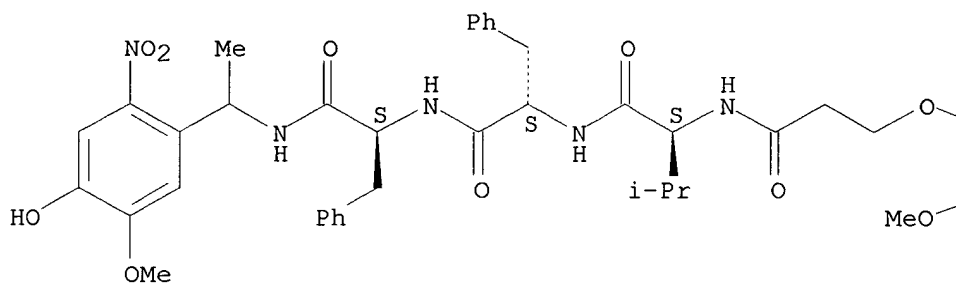


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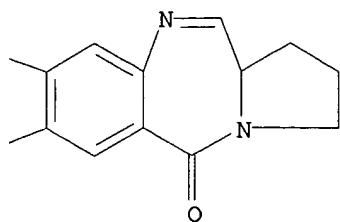
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Absolute stereochemistry.

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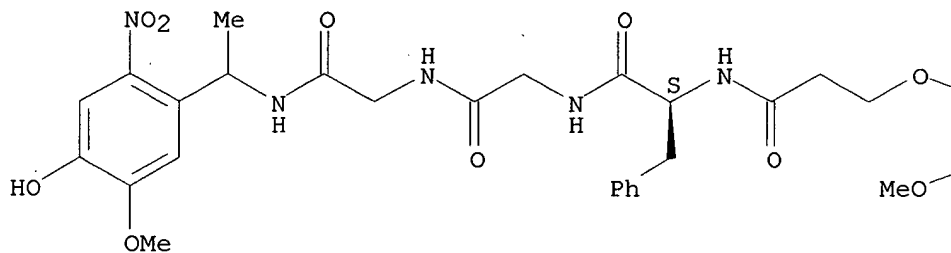


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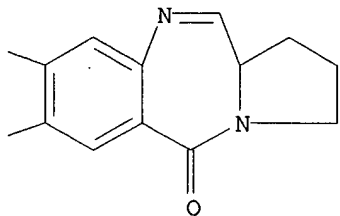
CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[1-(4-hydroxy-5-methoxy-2-nitrophenyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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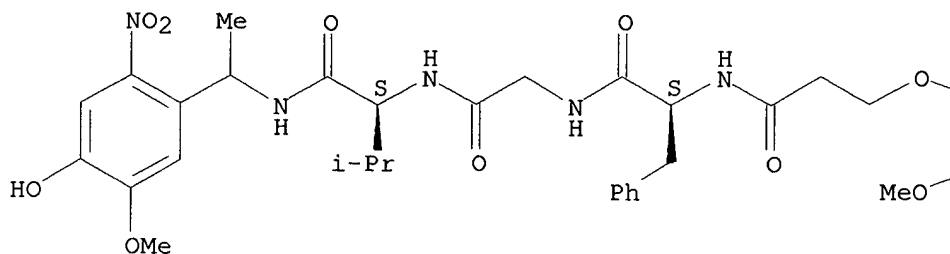


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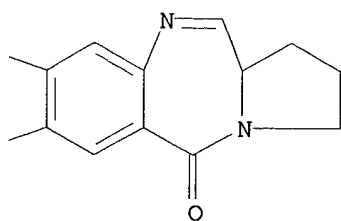
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Absolute stereochemistry.

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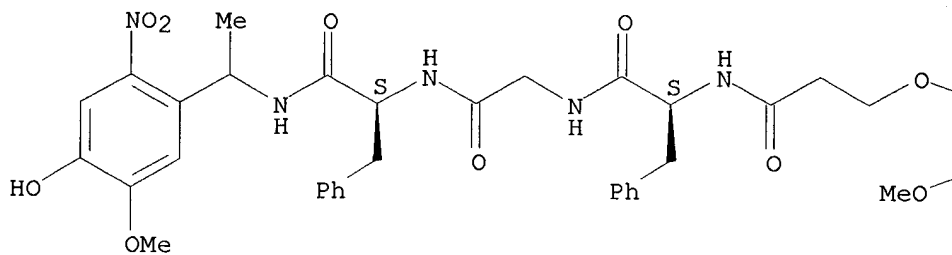


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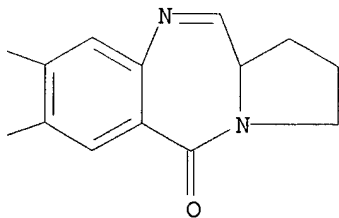
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Absolute stereochemistry.

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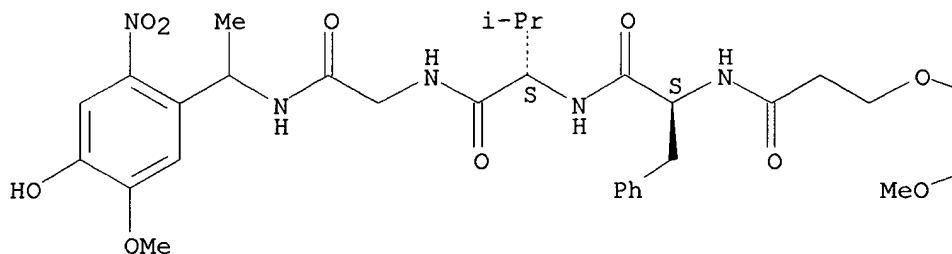
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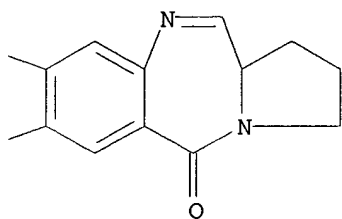
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Absolute stereochemistry.

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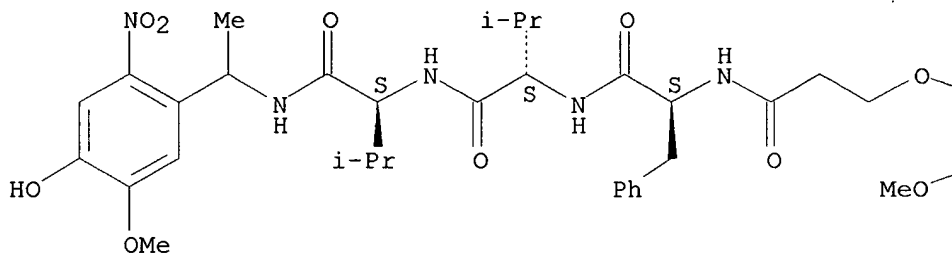


RN 260449-94-3 CAPLUS

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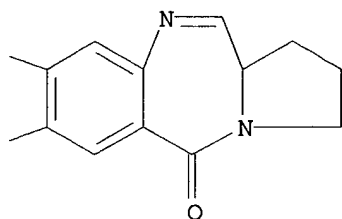
Absolute stereochemistry.

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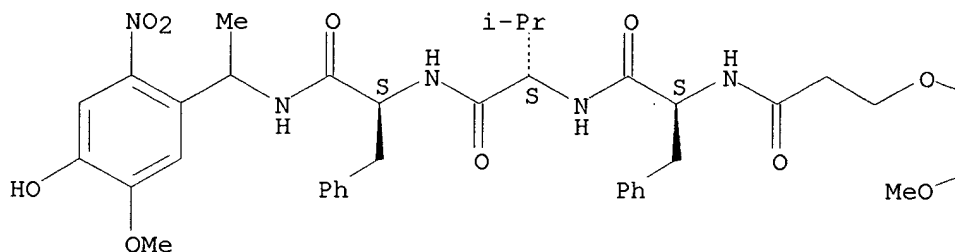


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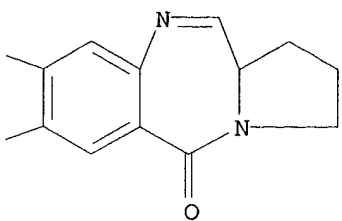
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Absolute stereochemistry.

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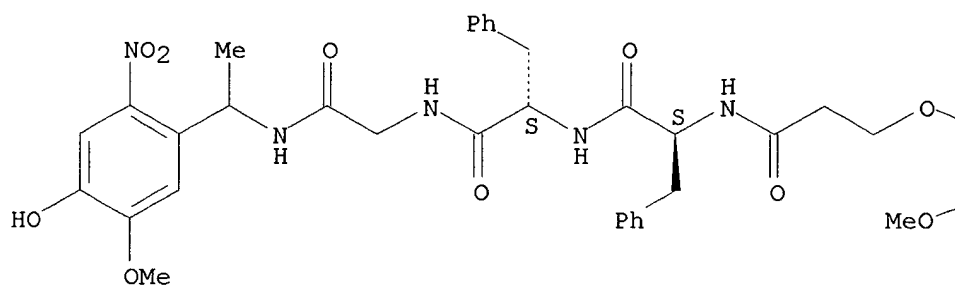


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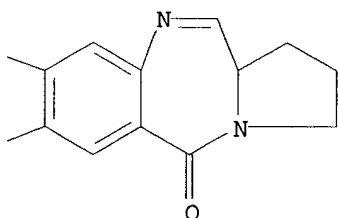
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Absolute stereochemistry.

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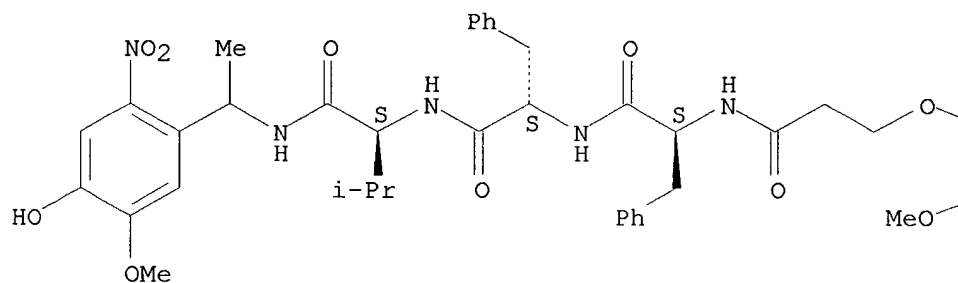


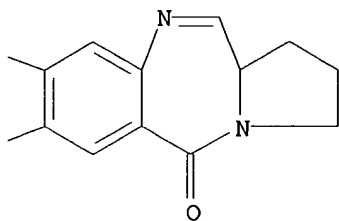
RN 260450-00-8 CAPLUS

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Absolute stereochemistry.

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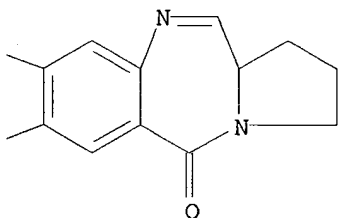
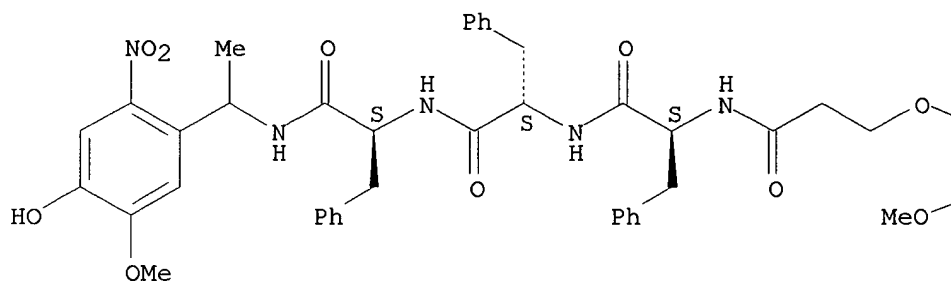




RN 260450-02-0 CAPLUS

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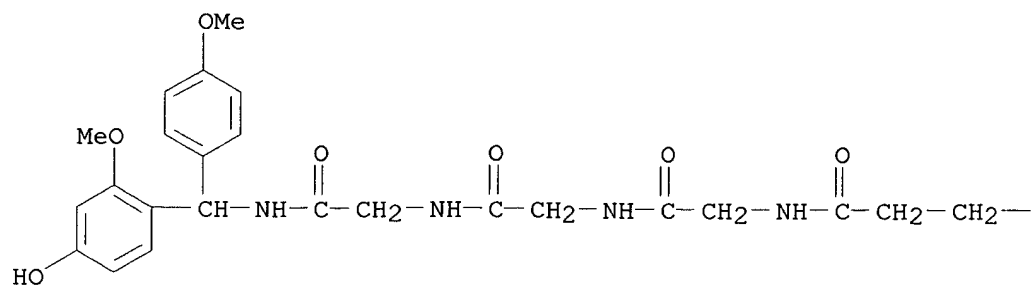
Absolute stereochemistry.



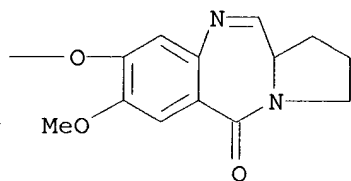
RN 260450-04-2 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B

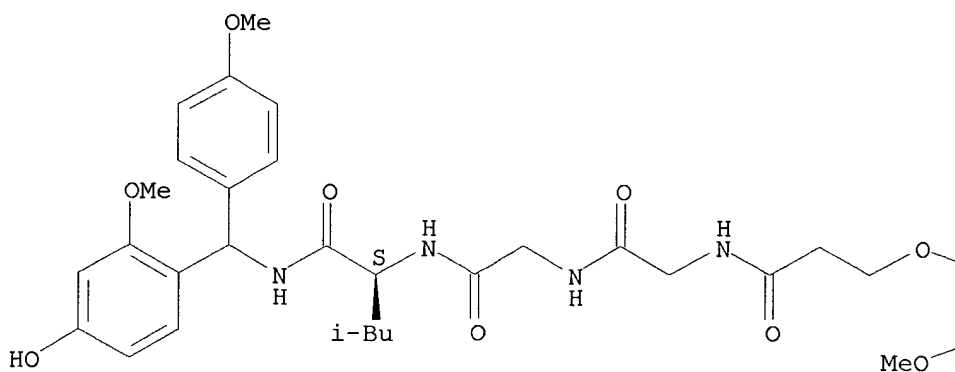


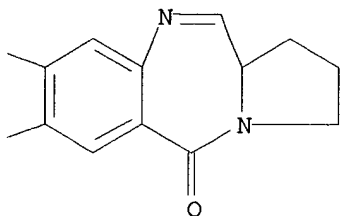
RN 260450-06-4 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

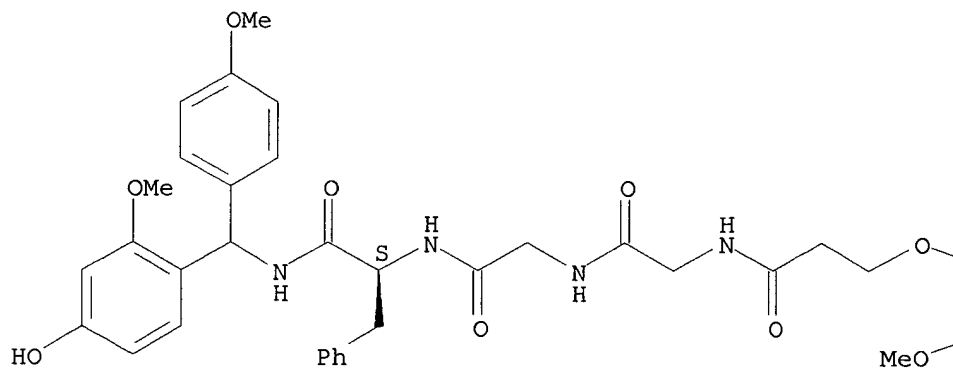


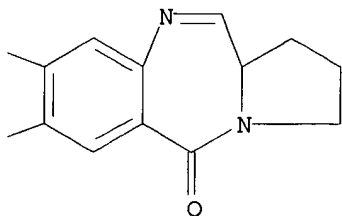


RN 260450-08-6 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

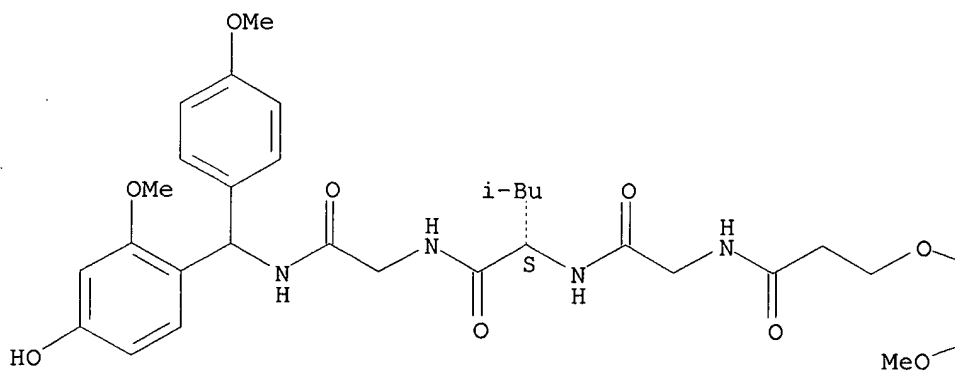


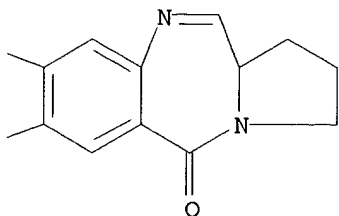


RN 260450-10-0 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

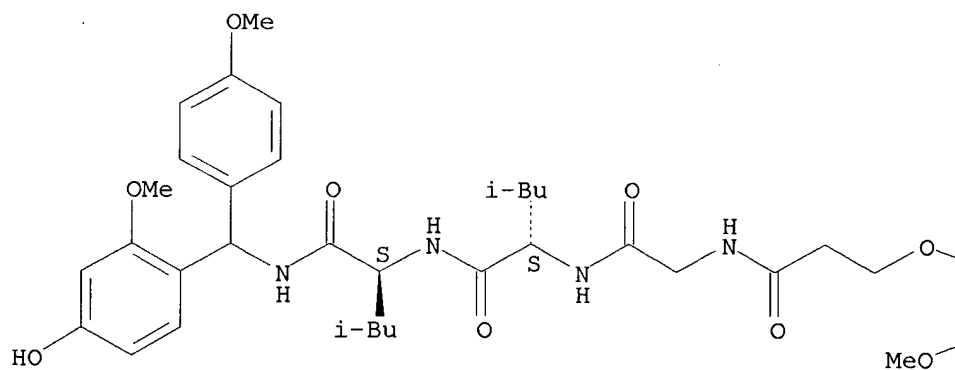


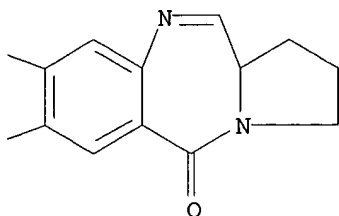


RN 260450-12-2 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

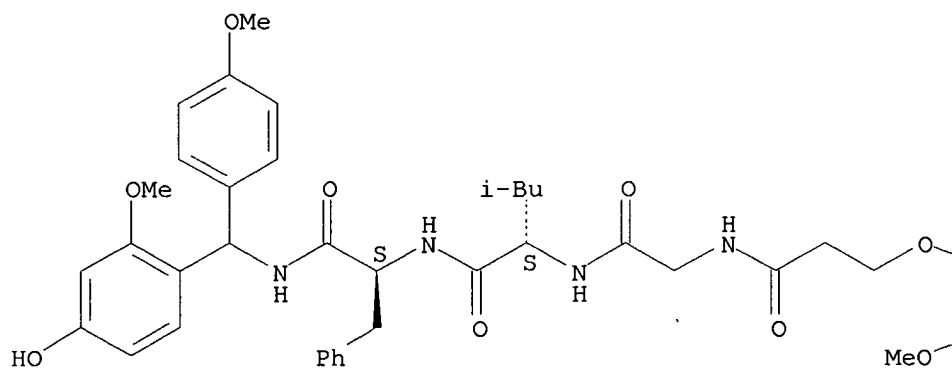




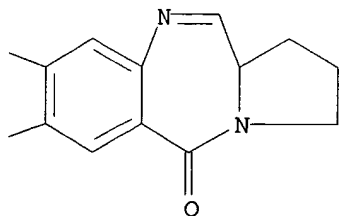
RN 260450-14-4 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



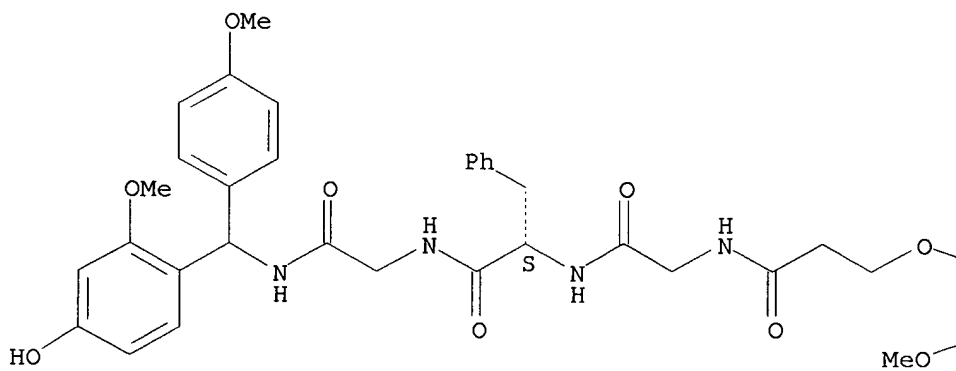


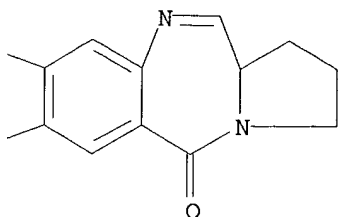


RN 260450-16-6 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

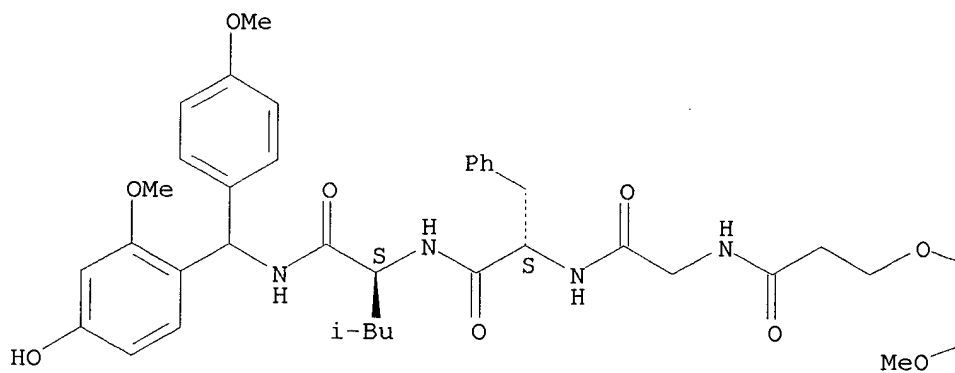


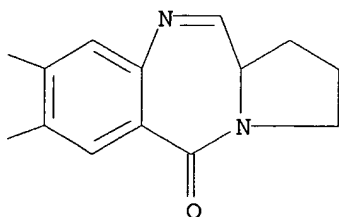


RN 260450-18-8 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

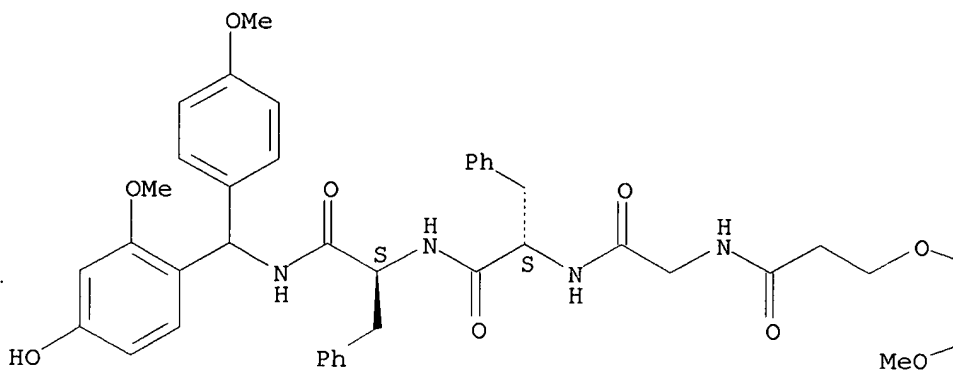


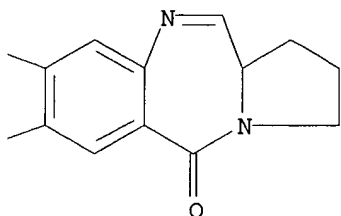


RN 260450-20-2 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]glycyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

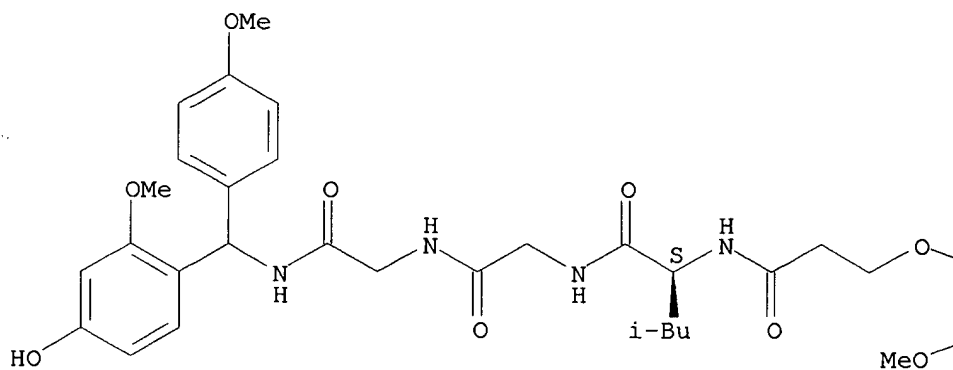


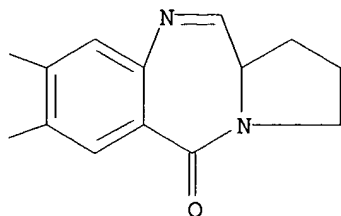


RN 260450-22-4 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

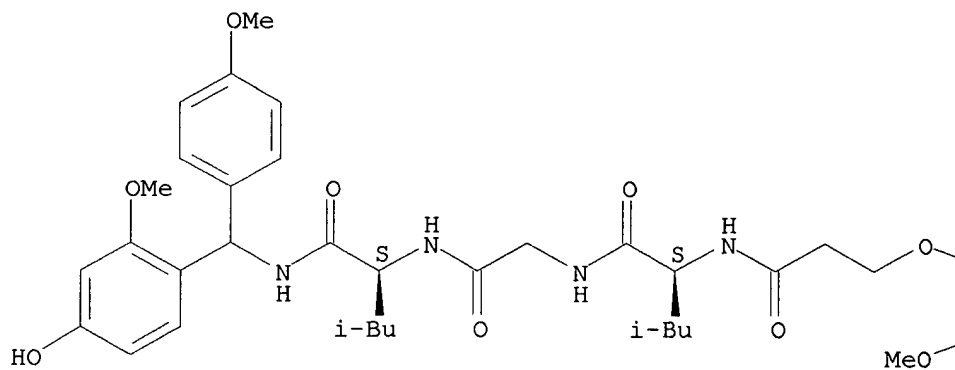


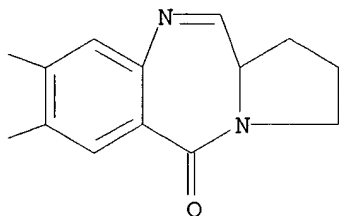


RN 260450-24-6 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

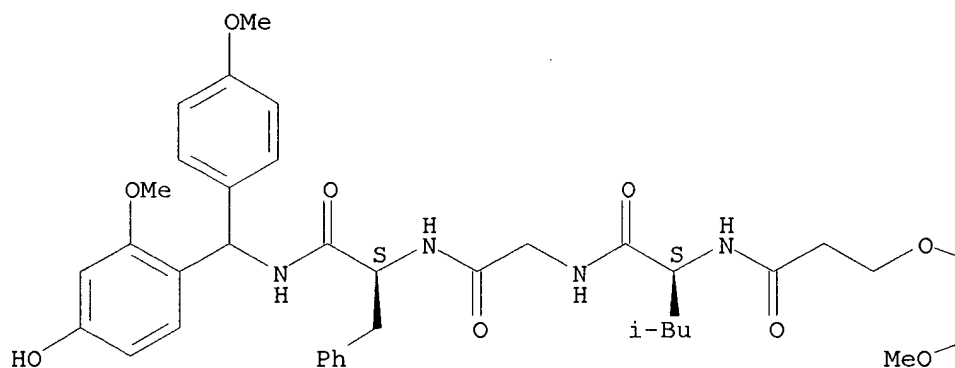


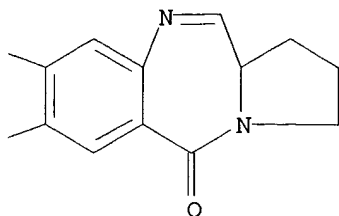


RN 260450-26-8 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

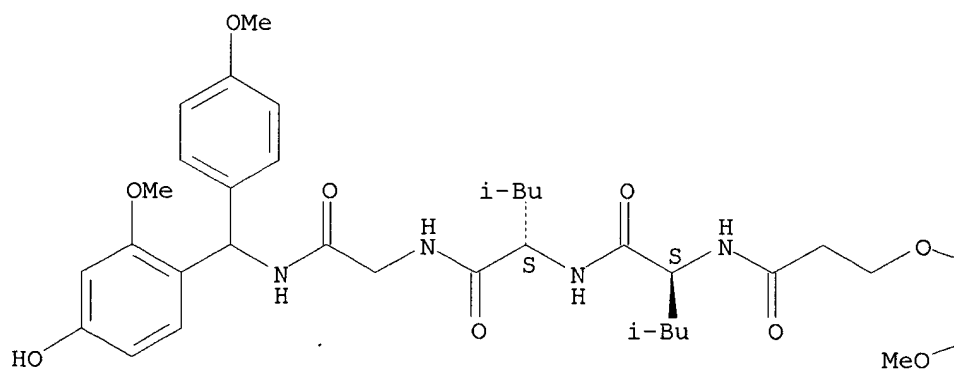


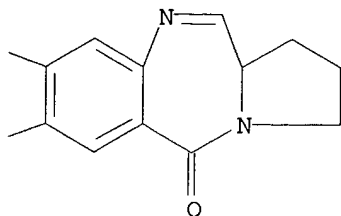


RN 260450-28-0 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

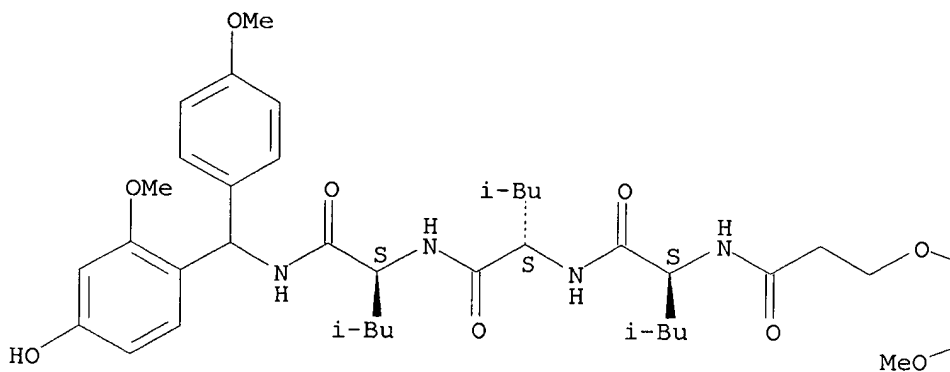




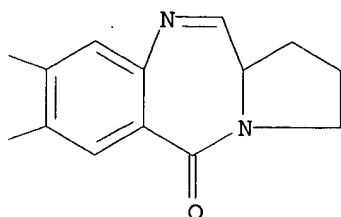
RN 260450-30-4 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



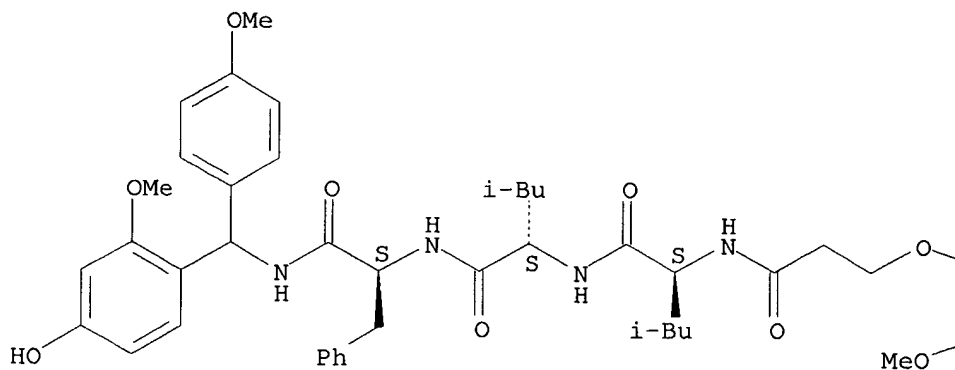


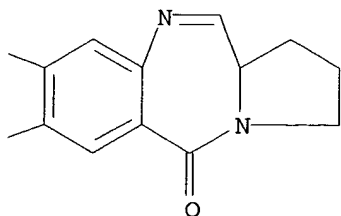


RN 260450-32-6 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

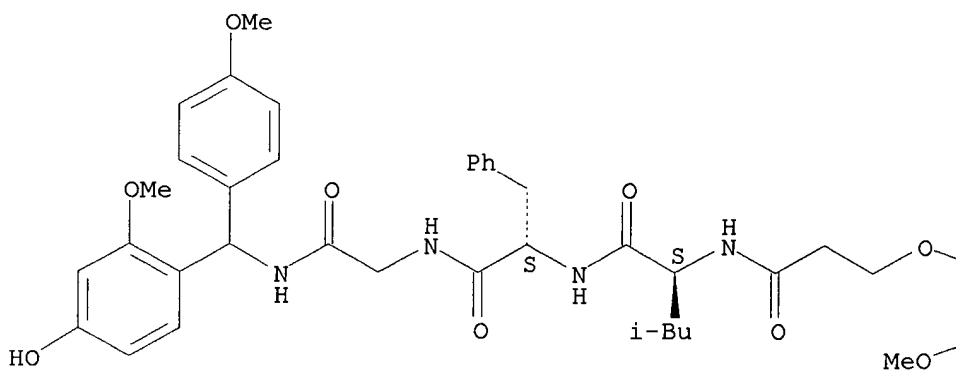


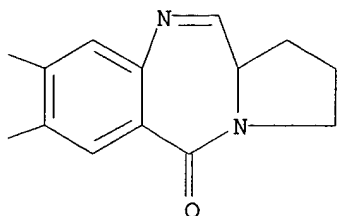


RN 260450-34-8 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

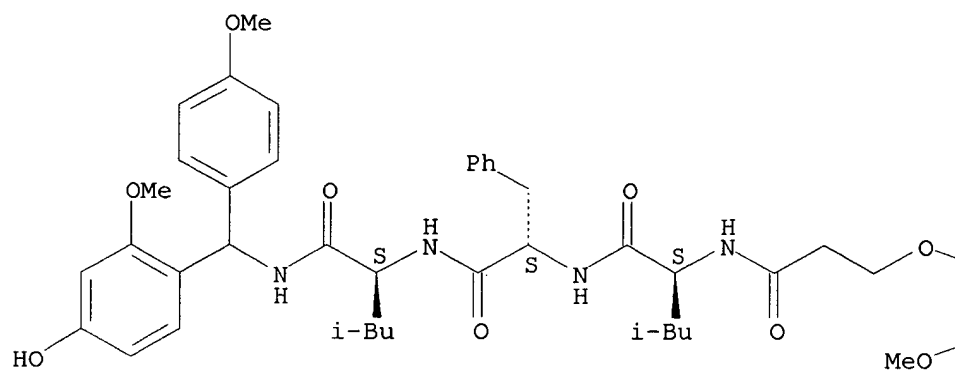


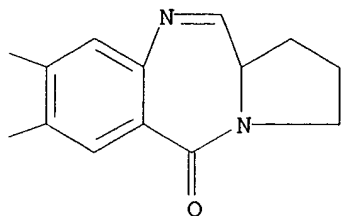


RN 260450-36-0 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

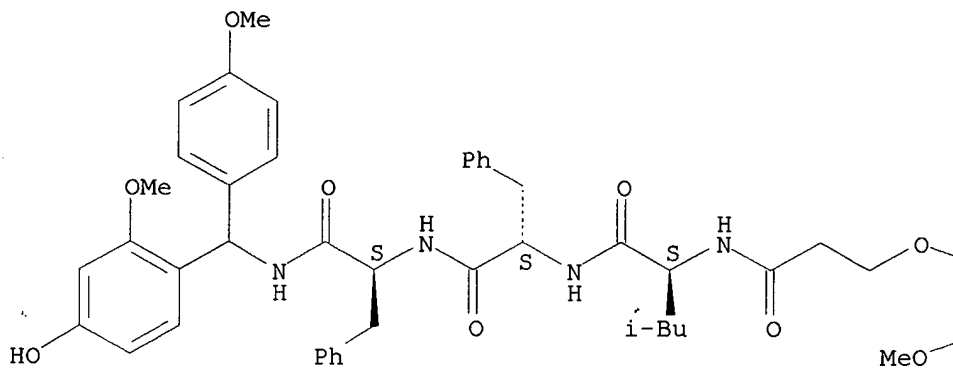


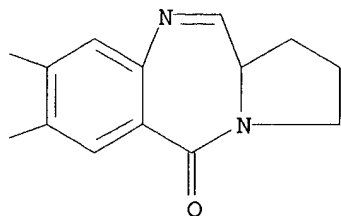


RN 260450-38-2 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-leucyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

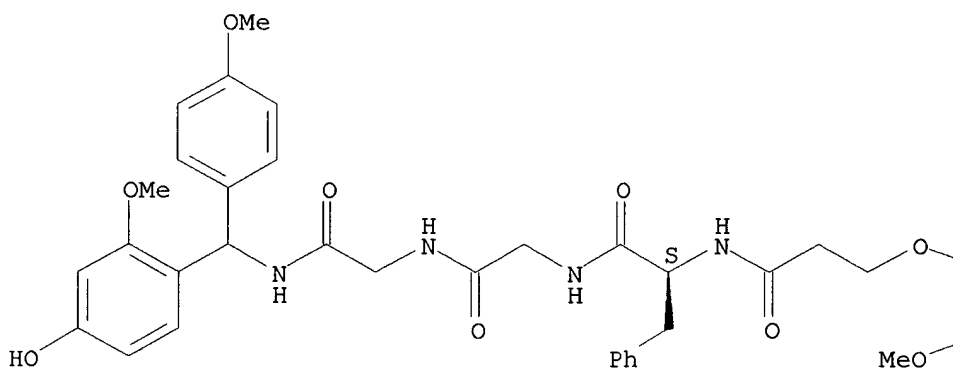


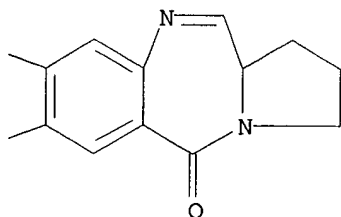


RN 260450-40-6 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

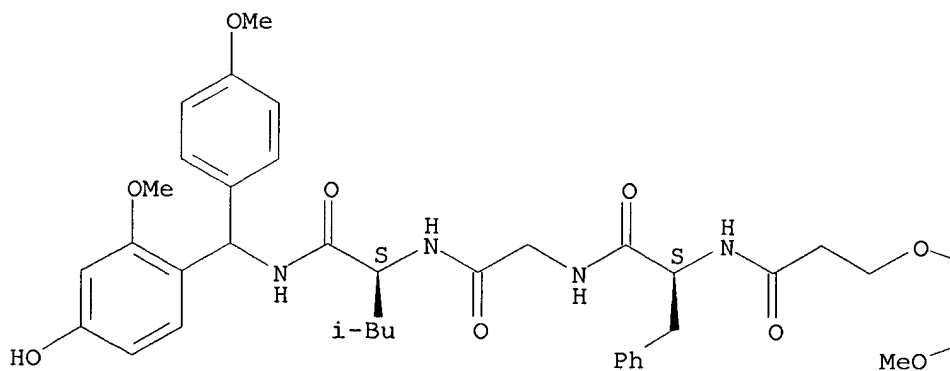


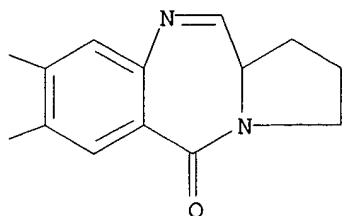


RN 260450-41-7 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-glycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

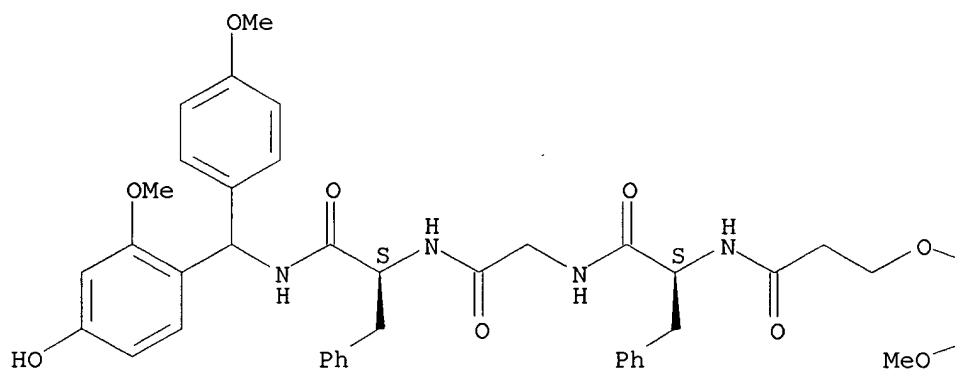


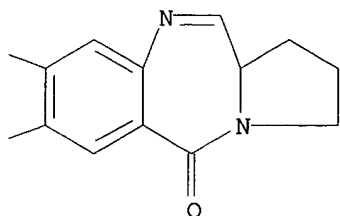


RN 260450-43-9 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanylglycyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

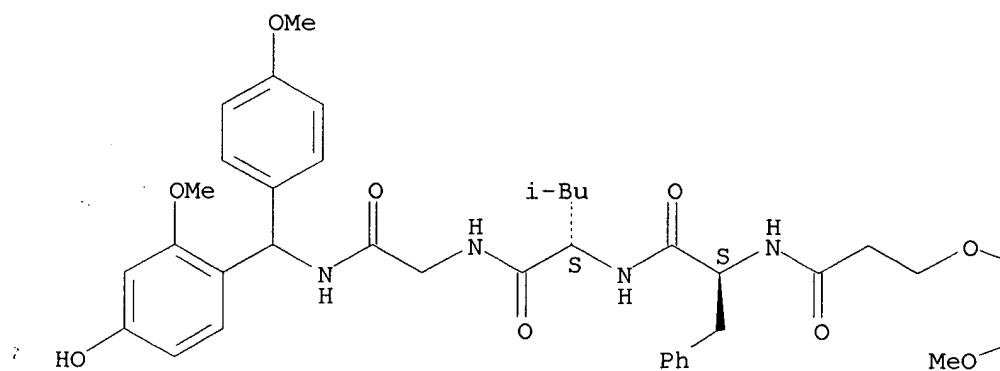




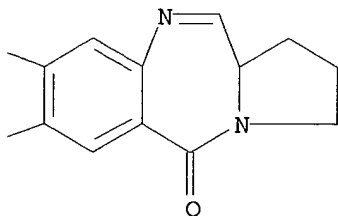
RN 260450-45-1 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



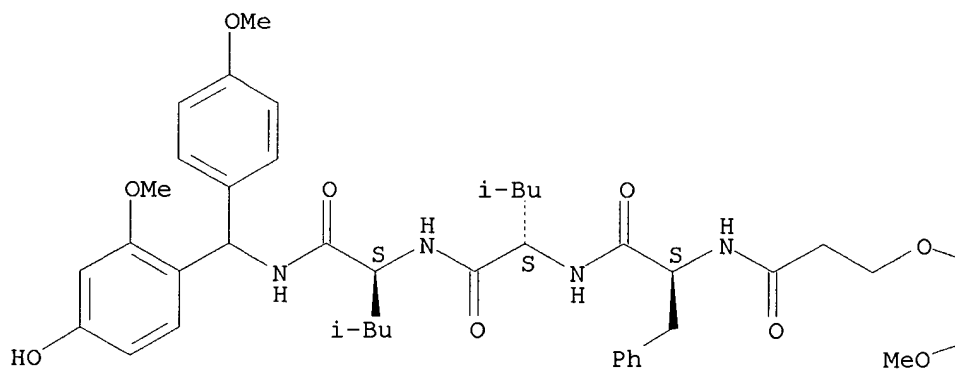


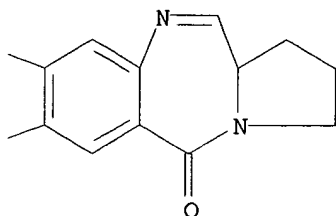


RN 260450-47-3 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

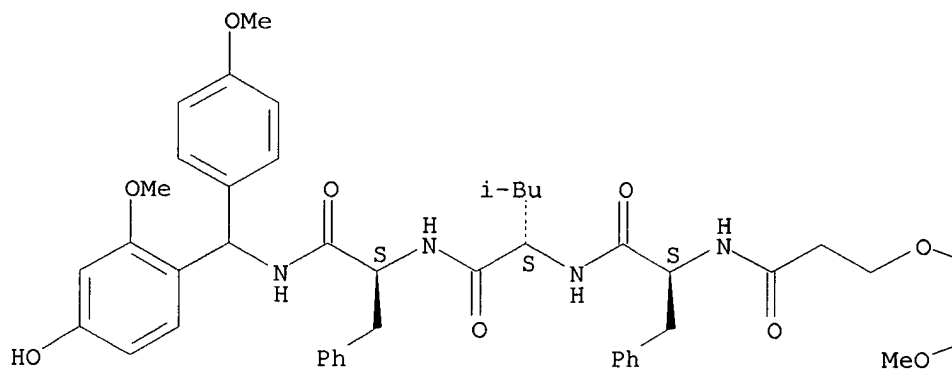


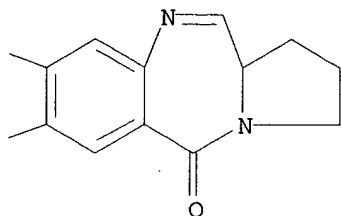


RN 260450-49-5 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-leucyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

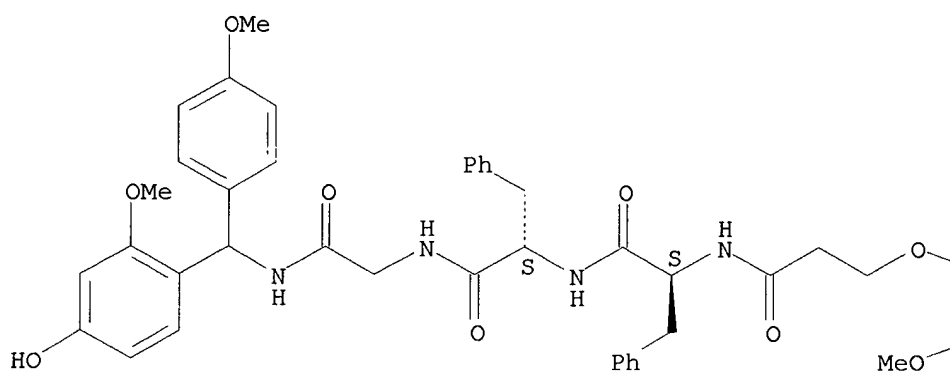


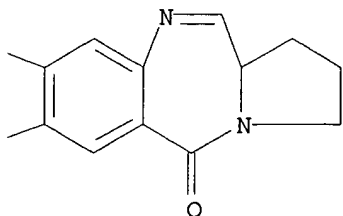


RN 260450-51-9 CAPLUS

CN Glycinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

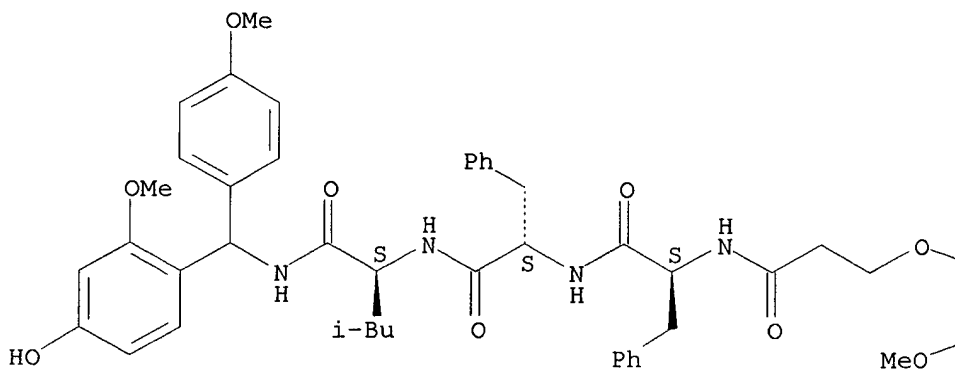


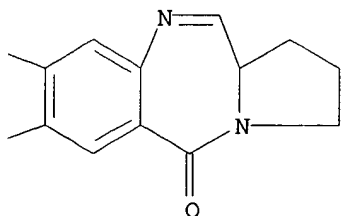


RN 260450-53-1 CAPLUS

CN L-Leucinamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

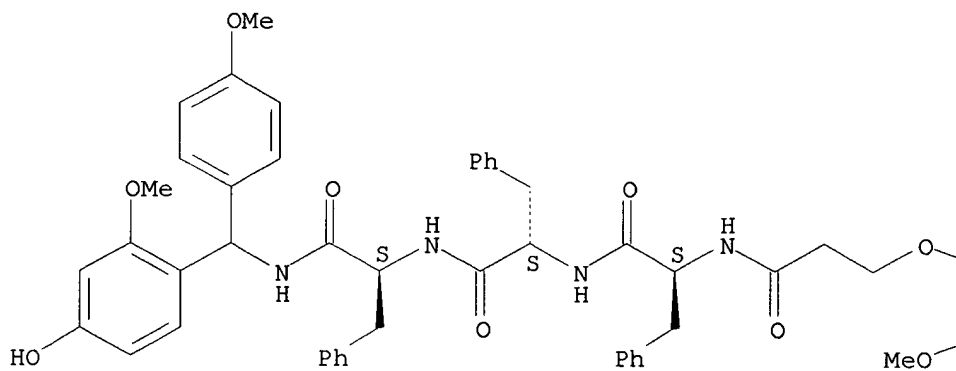


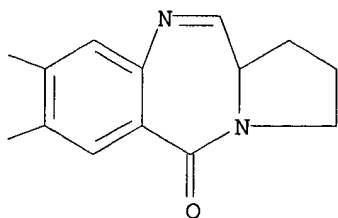


RN 260450-54-2 CAPLUS

CN L-Phenylalaninamide, N-[1-oxo-3-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]propyl]-L-phenylalanyl-L-phenylalanyl-N-[(4-hydroxy-2-methoxyphenyl)(4-methoxyphenyl)methyl]- (9CI)  
(CA INDEX NAME)

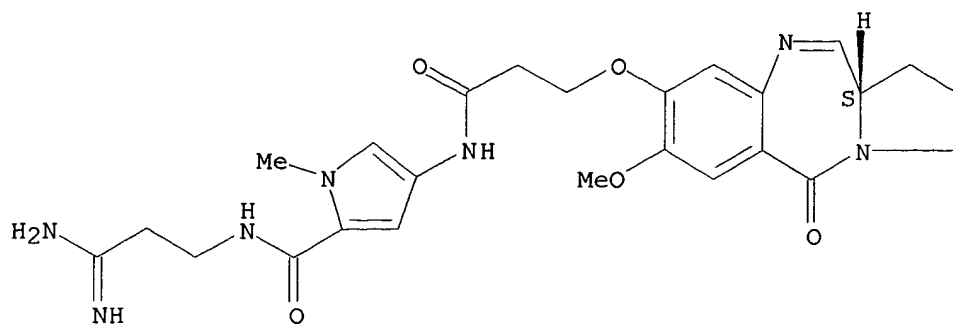
Absolute stereochemistry.





126 ANSWER 5 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1999:758546 CAPLUS  
 DN 132:137361  
 TI Synthesis, in Vitro Antiproliferative Activity, and DNA-Binding Properties of Hybrid Molecules Containing Pyrrolo[2,1-c][1,4]benzodiazepine and Minor-Groove-Binding Oligopyrrole Carriers  
 AU Baraldi, Pier Giovanni; Balboni, Gianfranco; Cacciari, Barbara; Guiotto, Andrea; Manfredini, Stefano; Romagnoli, Romeo; Spalluto, Giampiero; Thurston, David E.; Howard, Philip W.; Bianchi, Nicoletta; Rutigliano, Cristina; Mischiati, Carlo; Gambari, Roberto  
 CS Dipartimento di Scienze Farmaceutiche e Dipartimento di Biochimica e Biologia Molecolare, Universita di Ferrara, Ferrara, 44100, Italy  
 SO J. Med. Chem. (1999), 42(25), 5131-5141  
 CODEN: JMCMAR; ISSN: 0022-2623 *Dec*  
 PB American Chemical Society  
 DT Journal  
 LA English  
 OS CASREACT 132:137361  
 AB The synthesis, biol. activity, and DNA-binding properties of a series of four pyrrolo[2,1-c][1,4]benzodiazepine (PBD) hybrids contg. polypyrrole side chains are described and structure-activity relationships examd. To investigate sequence selectivity and stability of drug/DNA complexes, DNase I footprinting and arrested polymerase chain reaction (PCR) were performed on human c-myc oncogene, estrogen receptor gene, and human immunodeficiency virus type 1 long terminal repeat (HIV-1 LTR) gene sequences. The antiproliferative activity of the hybrids was tested in vitro on human myeloid leukemia K562 and T-lymphoid Jurkat cell lines and compared to antiproliferative effects of the natural product distamycin A 1, its tetrapyrrole homolog, DC 81, and a PBD ester. The new hybrids exhibit different DNA-binding activity with respect to both distamycin A 1 and the parent PBD. In addn., a direct relationship was found between the no. of pyrrole rings present in the hybrids and the stability of drug/DNA complexes. With respect to antiproliferative effects, it was found that the increase in the length of the polypyrrole backbone leads to an increase of in vitro antiproliferative effects, i.e., the hybrid with 4 pyrroles is more active than the other ones both against K562 and Jurkat cell lines.  
 IT **256949-67-4P 256949-68-5P 256949-69-6P 256949-70-9P**  
 RL: BAC (Biological activity or effector, except adverse); PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)  
 (prepn., antiproliferative activity, and DNA-binding pyrrolobenzodiazepines contg. oligopyrrole carriers)  
 RN 256949-67-4 CAPLUS  
 CN 1H-Pyrrole-2-carboxamide, N-(3-amino-3-iminopropyl)-1-methyl-4-[[1-oxo-3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



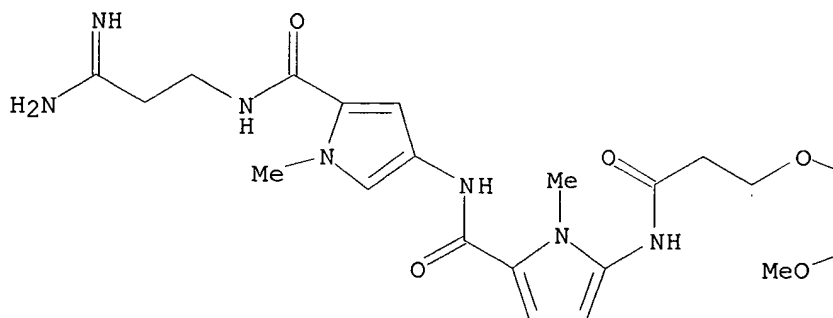
● HCl

RN 256949-68-5 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-(3-amino-3-iminopropyl)-1-methyl-4-[[[1-methyl-5-[[1-oxo-3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

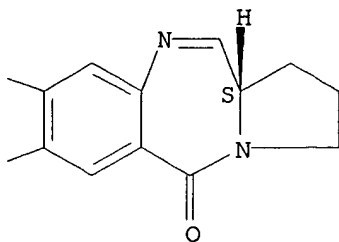
Absolute stereochemistry.

PAGE 1-A



● HCl

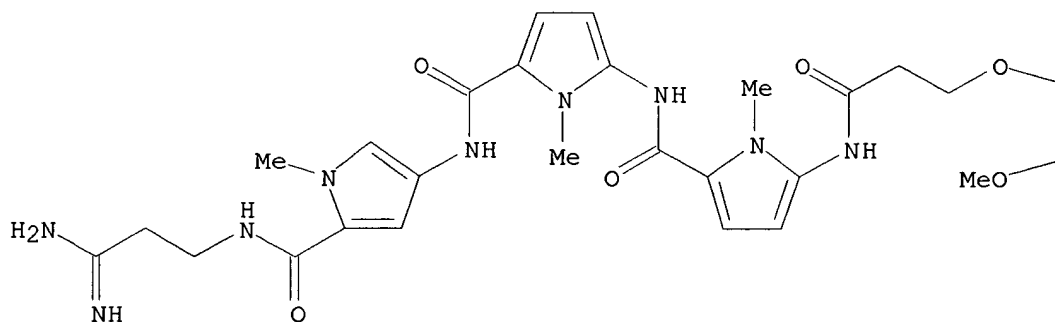




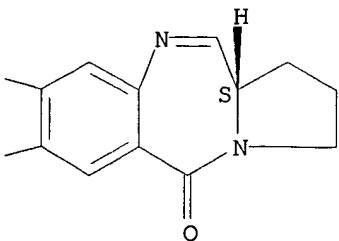
RN 256949-69-6 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[5-[[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl-5-[[[1-methyl-5-[[1-oxo-3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

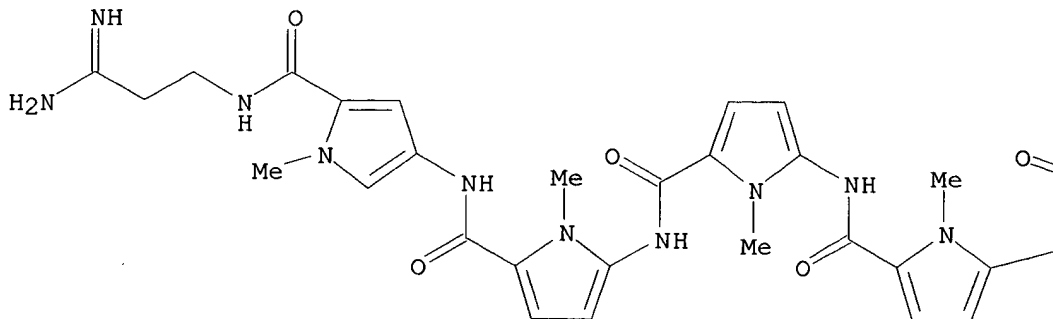


09/763,767

RN 256949-70-9 CAPLUS  
CN 1H-Pyrrole-2-carboxamide, N-[5-[[[5-[(3-amino-3-  
iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]amino]carbonyl]-1-  
methyl-1H-pyrrol-2-yl]-1-methyl-5-[[[1-methyl-5-[[1-oxo-3-[(11aS)-  
2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-  
yl]oxy]propyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-, monohydrochloride  
(9CI) (CA INDEX NAME)

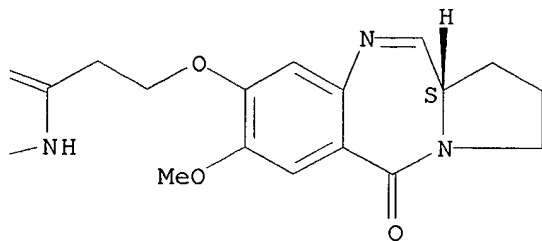
Absolute stereochemistry.

PAGE 1-A



● HCl

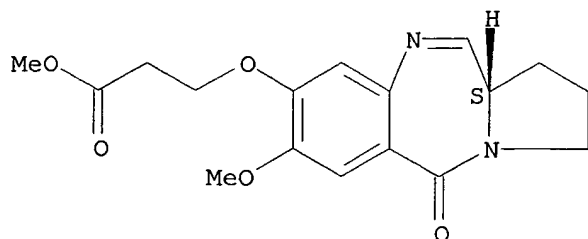
PAGE 1-B



IT 219562-69-3P  
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);  
SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn., antiproliferative activity, and DNA-binding  
pyrrolobenzodiazepines contg. oligopyrrole carriers)  
RN 219562-69-3 CAPLUS  
CN Propanoic acid, 3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-  
pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]-, methyl ester (9CI) (CA INDEX  
NAME)

09/763,767

Absolute stereochemistry. Rotation (+).



RE.CNT 39

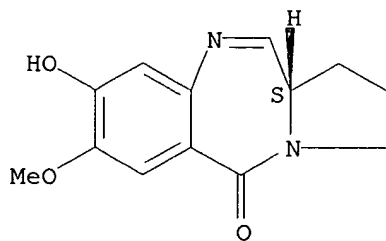
RE

- (1) Arcamone, F; Gazz Chim Ital 1967, V97, P1097 CAPLUS
  - (2) Arcamone, F; Giorn Microbiol 1961, V9, P83 CAPLUS
  - (4) Baraldi, P; Bioorg Med Chem Lett 1998, V8, P3019 CAPLUS
  - (5) Baraldi, P; Curr Pharm Des 1998, V4, P249 CAPLUS
  - (6) Bentley, D; Mol Cell Biol 1986, V6, P3481 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/763,767

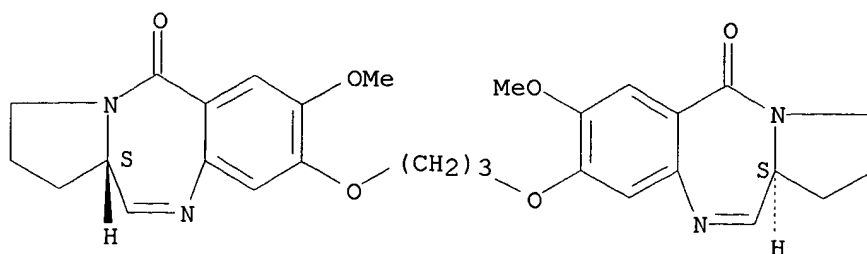
~~126~~ ANSWER 6 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1999:676295 CAPLUS  
DN 132:18480  
TI Molecular modeling of a sequence-specific DNA-binding agent based on the  
pyrrolo[2,1-c][1,4]benzodiazepines  
AU Adams, Lesley J.; Jenkins, Terence C.; Banting, Lee; Thurston, David E.  
CS CRC Gene Targeted Drug Design Research Group, School of Pharmacy and  
Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, UK  
SO Pharm. Pharmacol. Commun. (1999), 5(9), 555-560  
CODEN: PPCOFN; ISSN: 1460-8081  
PB Royal Pharmaceutical Society of Great Britain  
DT Journal  
LA English  
AB The CHARMM force field was used for the first time to model the tricyclic  
pyrrolobenzodiazepine (PBD) ring system. This system forms the core of  
the well known sequence-selective DNA-interactive anthramycin-type  
antitumor antibiotics. The results agreed with previous results obtained  
using the AMBER and X-PLOR force fields. The simple family member DC-81  
preferentially binds in the 5S orientation with S-stereochem. at the C11  
position of the PBD and with the A-ring of the mol. oriented towards the  
5' end of the covalently bound strand. The modeling studies and energetic  
analyses also support the observation that the mols. have a sequence  
preference for the purine-guanine-purine motif.  
IT 81307-24-6, DC-81 140676-21-7, DSB-120  
RL: BAC (Biological activity or effector, except adverse); PRP  
(Properties); BIOL (Biological study)  
(mol. modeling of a sequence-specific DNA-binding agent based on the  
pyrrolo[2,1-c][1,4]benzodiazepines)  
RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 140676-21-7 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-  
propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 14

RE

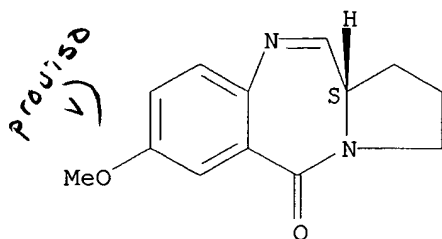
- (1) Adams, L; Pharm Sci 1995, V1, P151 CAPLUS
- (2) Arora, S; Acta Cryst 1979, VB35, P2945 CAPLUS
- (3) Brooks, B; J Comp Chem 1983, V4, P187 CAPLUS
- (4) Fletcher, D; J Chem Inf Comp Sci 1996, V36, P746 CAPLUS
- (5) Jenkins, T; Eur J Biochem 1993, V213, P1175 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/763,767

~~L26~~ ANSWER 7 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1999:615557 CAPLUS  
DN 132:207668  
TI New methods for the synthesis of natural products  
AU Melekhov, Alexey G.  
CS Iowa State Univ., Ames, IA, USA  
SO (1999) 83 pp. Avail.: UMI, Order No. DA9924747  
From: Diss. Abstr. Int., B 1999, 60(4), 1613  
DT Dissertation  
LA English  
AB Unavailable  
IT **133954-34-4P**, 8-Deoxy-DC-81  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(new methods for the synthesis of natural products)  
RN 133954-34-4 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-  
, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



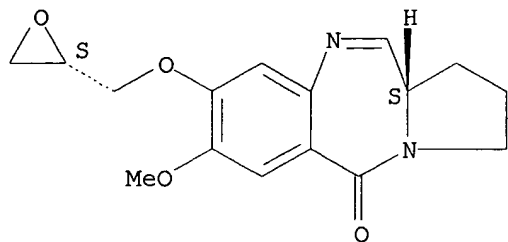
form. III

09/763,767

~~LI~~6 ANSWER 8 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1999:583940 CAPLUS  
DN 132:89603  
TI Design, Synthesis, and Evaluation of a Novel Sequence-Selective  
Epoxide-Containing DNA Cross-Linking Agent Based on the  
Pyrrolo[2,1-c][1,4]benzodiazepine System  
AU Wilson, Stuart C.; Howard, Philip W.; Forrow, Stephen M.; Hartley, John  
A.; Adams, Lesley J.; Jenkins, Terence C.; Kelland, Lloyd R.; Thurston,  
David E.  
CS CRC Gene Targeted Drug Design Research Group School of Pharmacy and  
Biomedical Sciences, University of Portsmouth, Hants., PO1 2DT, UK  
SO J. Med. Chem. (1999), 42(20), 4028-4041  
CODEN: JMCMAR; ISSN: 0022-2623 Oct.  
PB American Chemical Society  
DT Journal  
LA English  
OS CASREACT 132:89603  
AB Synthetic routes have been investigated to prep. a novel  
C8-epoxide-functionalized pyrrolo[2,1-c][1,4]benzodiazepine 1 as a  
potential sequence-selective DNA crosslinking agent (Wilson et al.  
Tetrahedron Lett. 1995, 36, 6333-6336). A successful synthesis was  
accomplished via a 10-step route involving a pro-N10-Fmoc cleavage method  
that should have general applicability to other pyrrolobenzodiazepine  
(PBD) mols. contg. acid- or nucleophile-sensitive groups. During the  
course of this work, a one-pot reductive cyclization procedure for the  
synthesis of PBD N10-C11 imines from nitro di-Me acetals was also  
discovered, although this method results in C11a racemization which can  
reduce DNA binding affinity and cytotoxicity. The target epoxide 1 was  
shown by thermal denaturation studies to have a significantly higher  
DNA-binding affinity than the parent DC-81 or the C8-propenoxy-PBD, which  
is structurally similar but lacks the epoxide moiety. The time course of  
effects upon thermal denaturation indicated a rapid initial binding phase  
followed by a slower phase consistent with the stepwise crosslinking of  
DNA obsd. for a difunctional agent. This was confirmed by an  
electrophoretic assay which demonstrated efficient induction of  
interstrand cross-links in plasmid DNA at concns. >1 .mu.M. Higher levels  
of interstrand crosslinking were obsd. at 24 h compared to 6 h incubation.  
A Taq polymerase stop assay indicated a preference for binding to  
guanine-rich sequences as predicted for bis-alkylation in the minor groove  
of DNA by epoxide and imine moieties. The pattern of stop sites could be  
partly rationalized by mol. modeling studies which suggested low-energy  
models to account for the obsd. binding behavior. The epoxide PBD 1 was  
shown to have significant cytotoxicity (45-60 nM) in the A2780, CH1, and  
CH1cisR human ovarian carcinoma cell lines and an IC50 of 0.2 .mu.M in  
A2780cisR. The significant activity of 1 in the cisplatin-resistant  
CH1cisR cell line (IC50 = 47 nM) gave a resistance factor of 0.8 compared  
to the parent cell line, demonstrating no cross-resistance with the major  
groove crosslinking agent cisplatin.  
IT **171002-52-1P**  
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or  
effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic  
use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(design, synthesis, and evaluation of novel sequence-selective  
epoxide-contg. DNA crosslinking agent based on pyrrolo[2,1-  
c][1,4]benzodiazepine system)  
RN 171002-52-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-  
8-[(2S)-oxiranylmethoxy]-, (11aS)- (9CI) (CA INDEX NAME)

09/763,767

Absolute stereochemistry.



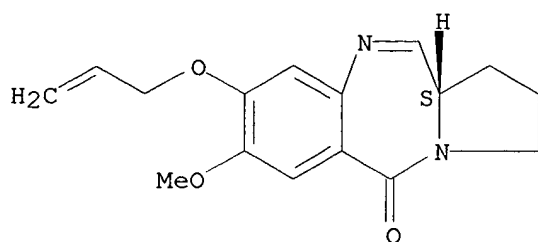
IT 251109-31-6P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(intermediate; prepn., thermal stability with CT-DNA, and in vitro cytotoxicity)

RN 251109-31-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(2-propenyloxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



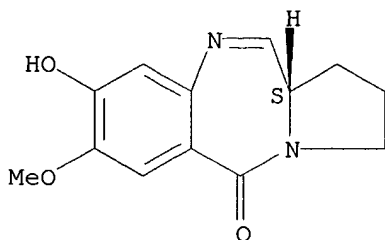
IT 81307-24-6, DC 81 140676-21-7, DSB 120

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(thermal stability with CT-DNA and in vitro cytotoxicity)

RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



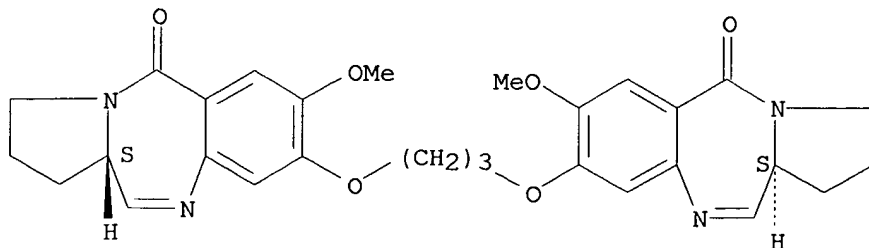
RN 140676-21-7 CAPLUS



09/763,767

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 59

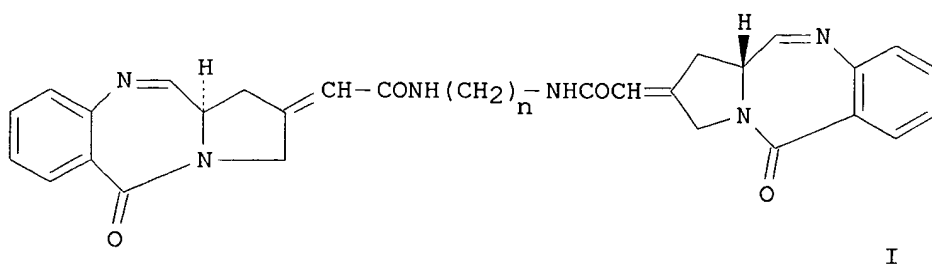
RE

- (1) Adams, L; Pharm Sci 1995, V1, P151 CAPLUS
- (2) Armstrong, R; J Am Chem Soc 1992, V114, P3144 CAPLUS
- (3) Arora, S; Acta Crystallogr 1979, VB35, P2945 CAPLUS
- (5) Bose, D; J Am Chem Soc 1992, V114, P4939 CAPLUS
- (8) Brooks, B; J Comput Chem 1983, V4, P187 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/763,767

✓  
LX6 ANSWER 9 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1999:444659 CAPLUS  
DN 131:199684  
TI Design and efficient synthesis of novel DNA interstrand crosslinking agents. C(2)-linked pyrrolo[2,1-c][1,4]benzodiazepine dimers  
AU Reddy, B. S. Praveen; Damayanthi, Yalamati; Lown, J. William  
CS Department Chemistry, Univ. Alberta, Edmonton, AB, T6G 2G2, Can.  
SO Synlett (1999), (7), 1112-1114  
CODEN: SYNLES; ISSN: 0936-5214  
PB Georg Thieme Verlag  
DT Journal  
LA English  
OS CASREACT 131:199684  
GI



AB The design and facile synthesis of C(2)-linked pyrrolo[2,1-c][1,4]benzodiazepines I ( $n = 3-5$ ) are described. The compds. are prepd. with varying degrees of linker length to probe the structural requirements for optimal DNA interstrand crosslinking. The products formed are exclusively of the E-configuration.

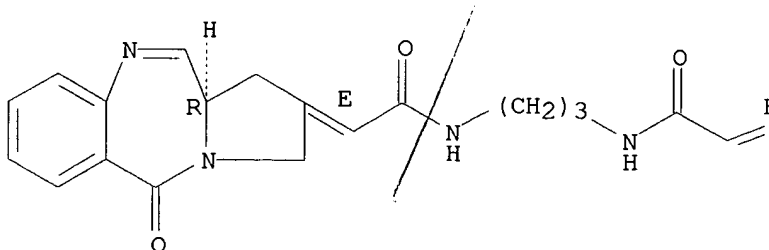
IT **241489-22-5P 241489-23-6P 241489-24-7P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of amide-linked pyrrolobenzodiazepine dimers)

RN 241489-22-5 CAPLUS

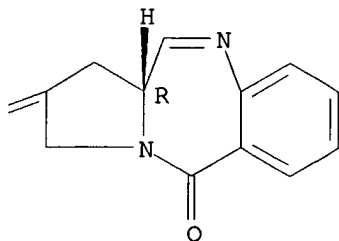
CN Acetamide, N,N'-1,3-propanediylbis[2-[(11aR)-5,11a-dihydro-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene]-, (2E,2'E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as described by E or Z.

PAGE 1-A



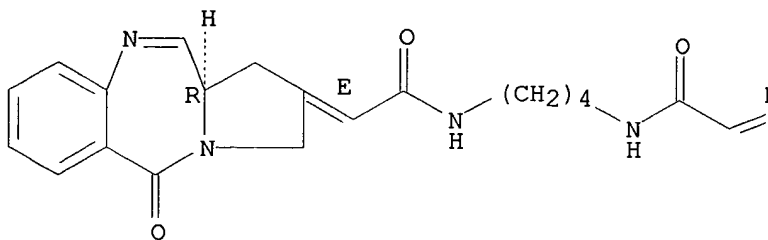
PAGE 1-B



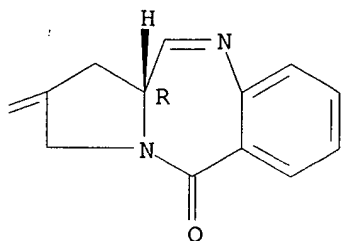
RN 241489-23-6 CAPLUS  
 CN Acetamide, N,N'-1,4-butanediylbis[2-[(11aR)-5,11a-dihydro-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene]-, (2E,2'E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as described by E or Z.

PAGE 1-A



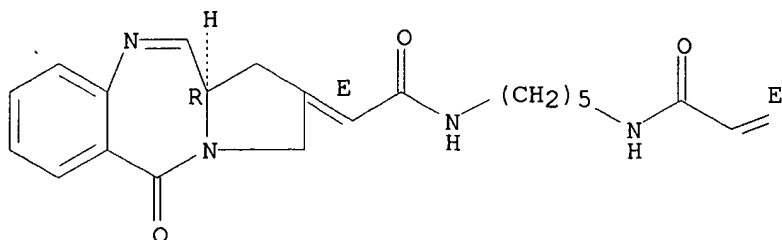
PAGE 1-B



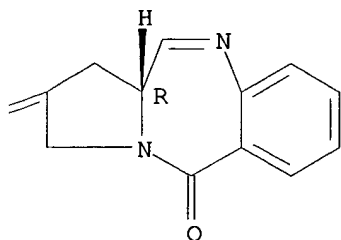
RN 241489-24-7 CAPLUS  
 CN Acetamide, N,N'-1,5-pentanediyibis[2-[(11aR)-5,11a-dihydro-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene]-, (2E,2'E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry as described by E or Z.

PAGE 1-A



PAGE 1-B



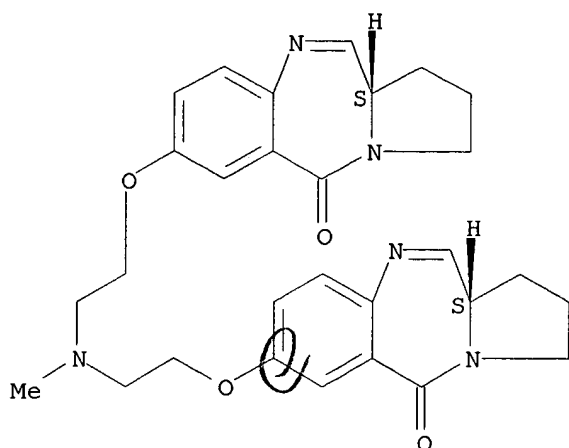
RE.CNT 13

RE

- (1) Bose, D; J Am Chem Soc 1992, V114, P4939 CAPLUS
  - (3) Dervan, P; Science 1986, V232, P464 CAPLUS
  - (4) Hurley, L; Chem Res Toxicol 1988, V1, P258 CAPLUS
  - (5) Hurley, L; Trends Pharmacol Res 1988, V9, P402 CAPLUS
  - (6) Mountzouris, J; J Med Chem 1994, V37, P3132 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

~~126~~ ANSWER 10 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1999:346781 CAPLUS  
~~DN~~ 131:140917  
 TI Biological effects of a bifunctional DNA cross-linker. II. Generation of micronuclei and attached micronuclear-like structures  
 AU Kurek, Kyle; Matsumoto, Lloyd; Gustafson, Gary; Pires, Richard; Tantravahi, Umadevi; Suggs, J. William  
 CS Division of Biology and Medicine, Brown University, Providence, RI, 02912, USA  
 SO Mutat. Res. (1999), 426(1), 89-94  
 CODEN: MUREAV; ISSN: 0027-5107  
 PB Elsevier Science B.V.  
 DT Journal  
 LA English  
 AB Madin-Darby bovine kidney (MDBK) cells were treated with the bifunctional DNA cross-linker, L-7, to examine the generation of micronuclei and other nuclear abnormalities. The preceding paper demonstrates that L-7 treatment induces the formation of triradial and quadriradial chromosomes in MDBK cells. These chromosomes are believed to result from interduplex DNA cross-links formed between G-C rich centromeric satellite DNA regions on non-sister chromatids. Treatment produces a majority of centromere-pos. micronuclei. In addn., many daughter cells remain attached by chromatin bridges which are sometimes beaded with micronuclei. Up to 15% of cell nuclei become lobular and fused with numerous micronuclear-like structures attached to their membranes. These attached structures are classified as attached micronuclear-like structures (AMNLS). Fluorescence in situ hybridization (FISH) using a centromeric satellite sequence was performed on treated cells. Hybridization reveals that intercellular bridges are composed of centromeric sequences and initiate at centromeric foci in daughter cells. Furthermore, the majority of junctions between AMNLS and nuclei contain an enhancement of centromeric signal. The frequency of AMNLS appears dependent on the concn. of L-7 and the duration of treatment. Similar results were found for the generation of cross-linked chromosome products in the previous paper. We suggest that AMNLS result from the abnormal mitotic segregation of cross-linked chromosome products.  
 IT **123064-64-2**  
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)  
 (biol. effects of bifunctional DNA cross-linker. II. Generation of micronuclei and attached micronuclear-like structures)  
 RN 123064-64-2 CAPLUS  
 CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,7'-[(methylimino)bis(2,1-ethanedioxy)]bis[1,2,3,11a-tetrahydro-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 29

RE

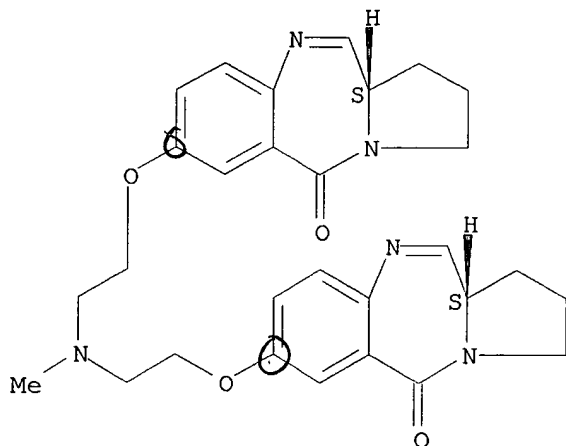
- (2) Brinkley, B; Aneuploidy: Etiology and Mechanisms 1985, V36, P243 CAPLUS
- (4) Charron, M; Chromosoma 1991, V100, P97 CAPLUS
- (5) Davidson, S; Eur J Cancer 1992, V28, P362 CAPLUS
- (6) Eastmond, D; Environ Mol Mutagen 1989, V13, P34 CAPLUS
- (7) Farmer, J; Nucleic Acids Res 1991, V19, P899 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/763,767

LS6 ANSWER 11 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1999:346774 CAPLUS  
DN 131:111396  
TI Biological effects of a bifunctional DNA crosslinker. I. Generation of  
triradial and quadriradial chromosomes  
AU Matsumoto, L.; Kurek, K.; Larocque, K.; Gustafson, G.; Pires, R.; Zhang,  
J.; Tantravahi, U.; Suggs, J. W.  
CS Department of Biology, Rhode Island College, Providence, RI, 02908-1991,  
USA  
SO Mutat. Res. (1999), 426(1), 79-87  
CODEN: MUREAV; ISSN: 0027-5107  
PB Elsevier Science B.V.  
DT Journal  
LA English  
AB Interduplex crosslinks by a bifunctional anthramycin DNA crosslinker  
produced triradial and quadriradial chromosomes. The crosslinker  
alkylates guanine at N-2. Bovine chromosomes contain GC-rich d. satellite  
DNAs at the centromeric heterochromatin and is the basis for the formation  
of triradial and quadriradial chromosomes at the centromeres. The in situ  
crosslinking of interphase chromosomes indicates that the distance between  
centromeres is 17.5 .ANG.. We conclude that the nuclear matrix assocd.  
DNA in the centromeric heterochromatin of interphase chromosomes are  
positioned close enough for crosslinking to occur. We propose a model for  
the generation of triradial and quadriradial chromosomes based upon the  
no. of interduplex crosslinks between two chromosomes.  
IT 123064-64-2  
RL: BAC (Biological activity or effector, except adverse); BUU (Biological  
use, unclassified); BIOL (Biological study); USES (Uses)  
(triradial and quadriradial chromosomes generated by the  
DNA-crosslinking agent L-7)  
RN 123064-64-2 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,7'-[(methylimino)bis(2,1-  
ethanediylxy)]bis[1,2,3,11a-tetrahydro-, (11aS,11'aS)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.



RE.CNT 30

RE

(1) Bodell, W; Mutat Res 1990, V233, P203 CAPLUS

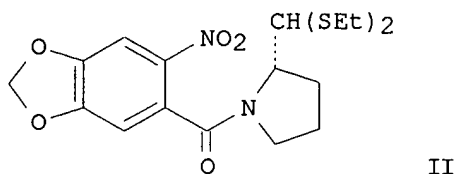
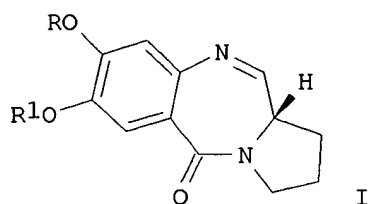
09/763,767

- (3) Brooks, B; Comput Chem 1983, V4, P187 CAPLUS
  - (5) Charron, M; Chromosoma 1991, V100, P97 CAPLUS
  - (8) Farmer, J; Nucleic Acids Res 1991, V19, P899 CAPLUS
  - (10) Fujiwara, Y; Br J Cancer 1993, V67, P1285 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT



09/763,767

~~L26~~ ANSWER 12 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1999:304467 CAPLUS  
DN 131:18989  
TI Effect of A-ring modifications on the DNA-binding behavior and  
cytotoxicity of pyrrolo[2,1-c][1,4]benzodiazepines  
AU Thurston, David E.; Bose, D. Subhas; Howard, Philip W.; Jenkins, Terence  
C.; Leoni, Alberto; Baraldi, Pier G.; Guiotto, Andrea; Cacciari, Barbara;  
Kelland, Lloyd R.; Foloppe, Marie-Paule; Rault, Sylvain  
CS CRC Gene Targeted Drug Design Research Group School of Pharmacy and  
Biomedical Sciences, University of Portsmouth, Portsmouth Hants, PO1 2DT,  
UK  
SO J. Med. Chem. (1999), 42(11), 1951-1964  
CODEN: JMCMAR; ISSN: 0022-2623  
PB American Chemical Society  
DT Journal  
LA English  
GI



AB Several A-ring-modified analogs of the DNA-binding antitumor agent DC-81 I (R = H, R1 = Me) have been synthesized in order to study structure-reactivity/cytotoxicity relationships. For two mols., the modifications required the addn. of a fourth ring to give the novel dioxolo[4,5-h]- and dioxano[5,6-h]pyrrolo[2,1-c][1,4]benzodiazepin-11-one (PBD) ring systems, resp. Another three analogs have the native benzenoid A-ring replaced with pyridine, diazine, or pyrimidine rings to give the novel pyrrolo[2,1-c][1,4]pyridodiazepine, pyrrolo[2,1-c][1,4]diazinodiazepine, and pyrrolo[2,1-c][1,4]pyrimidinodiazepine systems, resp. The other new analogs have extended chains at the C8-position of the DC-81 structure. During the synthesis of these compds., a novel tin-mediated regiospecific cleavage reaction of the dioxole intermediate II was discovered, leading to the previously unknown iso-DC-81 I (R = Me, R1 = H). In addn., an unusual simultaneous nitration-oxidn. reaction of 4-(3-hydroxypropoxy)-3-methoxybenzoic acid was found to produce 3-(4-carboxy-2-methoxy-5-nitrophenoxy)propanoic acid, a key intermediate, in high yield. In general, the results of cytotoxicity and DNA-binding studies indicated that none of the changes made to the A-ring of the PBD system significantly improved either binding affinity or cytotoxicity in comparison to DC-81. This result suggests that the superior potency of natural products such as anthramycin, tomaymycin, and sibiromycin is due entirely to differences in C-ring structure, and in particular exo or endo unsatn. at the C2-position and C2-substituents contg. unsatn. This study also provided information regarding the influence of A-ring substitution pattern on the relative stability of the interconvertible N10-C11 carbinolamine, carbinolamine Me ether, and imine forms of PBDs.

09/763,767

IT 72435-89-3 81307-24-6 81422-30-2

127810-79-1 226559-61-1

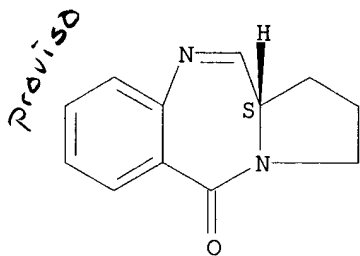
RL: BAC (Biological activity or effector, except adverse); BIOL  
(Biological study)

(prepn., cytotoxicity, and DNA-binding behavior of  
pyrrolobenzodiazepines)

RN 72435-89-3 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

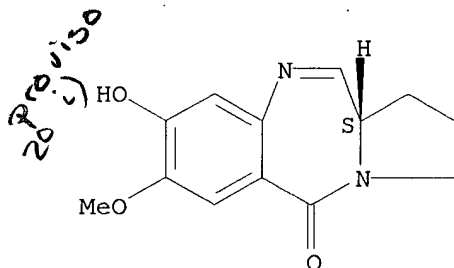


Form III

RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

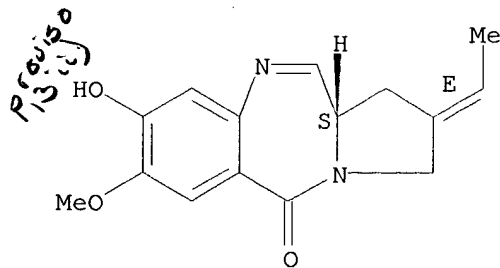


RN 81422-30-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-  
tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



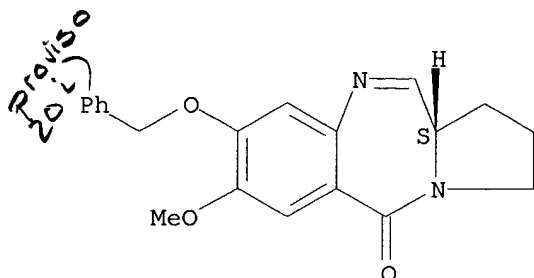
Form II

09/763,767

RN 127810-79-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

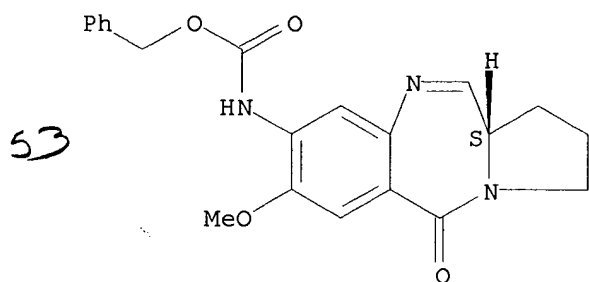
Absolute stereochemistry. Rotation (+).



RN 226559-61-1 CAPLUS

CN Carbamic acid, [(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



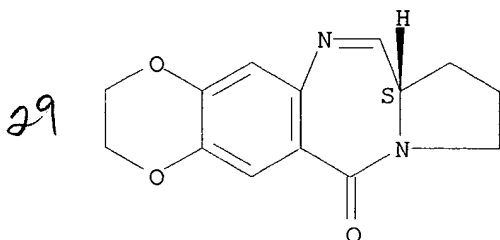
IT 226559-42-8P

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn., cytotoxicity, and DNA-binding behavior of pyrrolobenzodiazepines)

RN 226559-42-8 CAPLUS

CN 12H-1,4-Dioxino[2,3-h]pyrrolo[2,1-c][1,4]benzodiazepin-12-one, 2,3,7a,8,9,10-hexahydro-, (7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 147778-99-2P 219562-69-3P 226559-38-2P

09/763,767

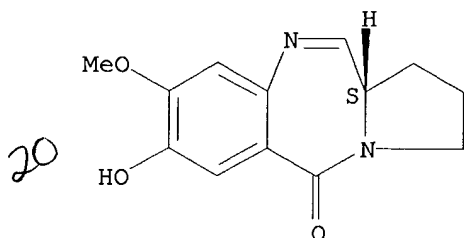
**226559-39-3P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn., cytotoxicity, and DNA-binding behavior of  
pyrrolobenzodiazepines)

RN 147778-99-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-hydroxy-8-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

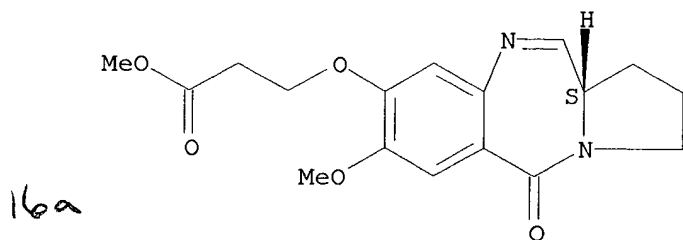
Absolute stereochemistry. Rotation (+).



RN 219562-69-3 CAPLUS

CN Propanoic acid, 3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

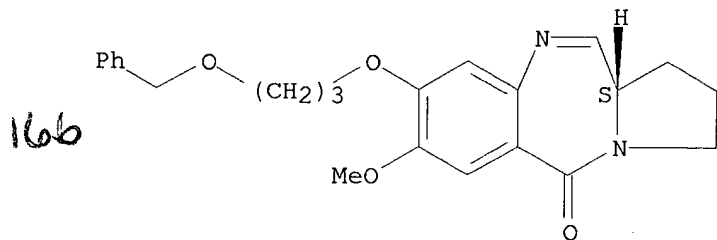
Absolute stereochemistry. Rotation (+).



RN 226559-38-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-[3-(phenylmethoxy)propoxy]-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

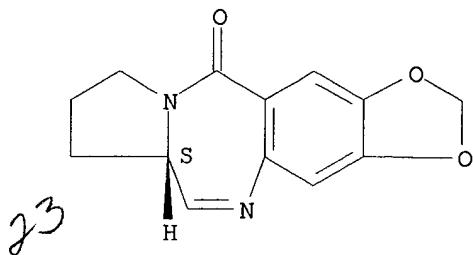


RN 226559-39-3 CAPLUS

09/763,767

CN 11H-1,3-Dioxolo[4,5-h]pyrrolo[2,1-c][1,4]benzodiazepin-11-one,  
6a,7,8,9-tetrahydro-, (6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 47

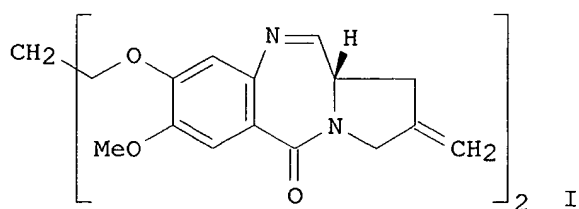
RE

- (1) Althuis, T; J Med Chem 1976, V20, P146 CAPLUS
- (2) Baraldi, P; J Med Chem 1994, V37, P4329 CAPLUS
- (3) Barkley, M; Biochemistry 1986, V25, P3021 CAPLUS
- (4) Beckwith, A; J Chem Soc C 1968, P2756 CAPLUS
- (5) Bock, L; US 2755273 1956 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

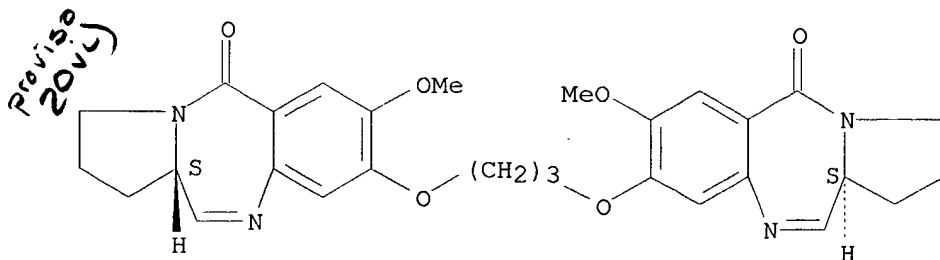
L26 ANSWER 13 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1999:273645 CAPLUS  
 DN 131:116218  
 TI Synthesis of a novel C2/C2'-exo unsaturated pyrrolobenzodiazepine cross-linking agent with remarkable DNA binding affinity and cytotoxicity  
 AU Gregson, Stephen J.; Howard, Philip W.; Thurston, David E.; Jenkins, Terence C.; Kelland, Lloyd R.  
 CS School of Pharmacy and Biomedical Sciences, CRC Gene Targeted Drug Design Research Group, University of Portsmouth, Portsmouth, Hants, PO1 2DT, UK  
 SO Chem. Commun. (Cambridge) (1999), (9), 797-798  
 CODEN: CHCOFS; ISSN: 1359-7345  
 PB Royal Society of Chemistry  
 DT Journal  
 LA English  
 GI

March



AB A C2/C2'-exo unsatd. pyrrolobenzodiazepine dimer (I) has been synthesized which is cytotoxic at the picomolar level and has remarkable covalent DNA binding affinity, raising the melting temp. of duplex-form calf thymus DNA by 34 after 18 h incubation.  
 IT **140676-21-7**, DSB-120  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)  
 (prepn. DNA binding and cytotoxicity of pyrrolobenzodiazepine crosslinking agents towards ovarian cancer cells)  
 RN 140676-21-7 CAPLUS  
 CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **232931-57-6P**  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

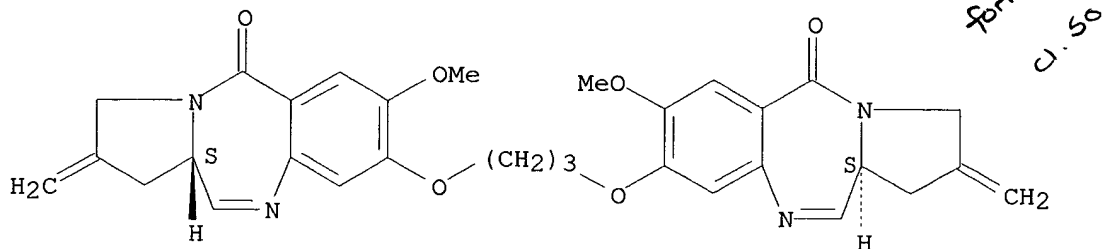
09/763,767

(prepn. DNA binding and cytotoxicity of pyrrolobenzodiazepine crosslinking agents towards ovarian cancer cells)

RN 232931-57-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-2-methylene-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 18

RE

- (1) Bose, D; J Am Chem Soc 1992, V114, P4939 CAPLUS
- (2) Dangles, O; J Org Chem 1987, V52, P4984 CAPLUS
- (3) Deziel, R; Tetrahedron Lett 1987, V28, P4371 CAPLUS
- (4) Fukuyama, T; Tetrahedron Lett 1993, V34, P2577 CAPLUS
- (5) Jenkins, T; J Med Chem 1994, V37, P4529 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/763,767

~~126~~ ANSWER 14 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1999:198610 CAPLUS

DN 131:5244

TI Hydride reductions of 1H-pyrrolo[2,1-c][1,4]-benzodiazepine-5,11-diones:  
selective reduction of secondary amides to carbinolamines

AU Katsifis, Andrew G.; McPhee, Meredith E.; Ridley, Damon D.

CS Biomedicine and Health Program, ANSTO, Menai, 2234, Australia

SO Aust. J. Chem. (1998), 51(12), 1121-1130

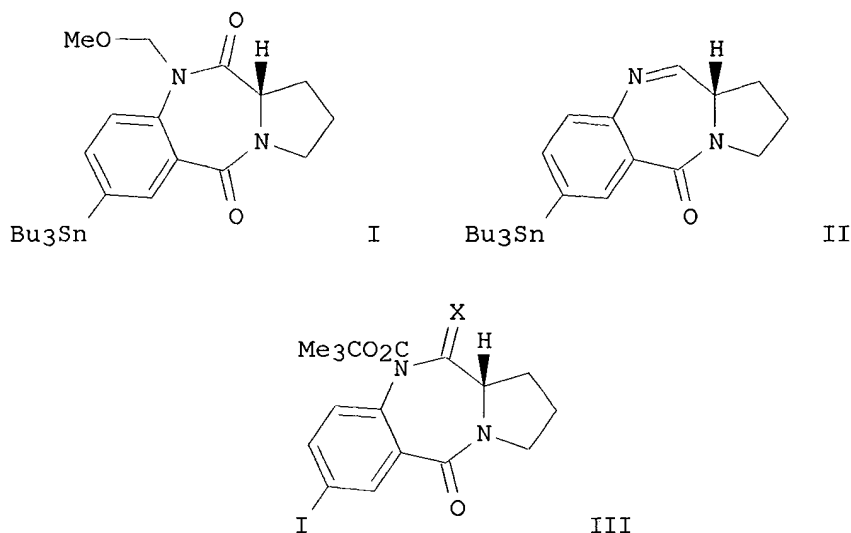
CODEN: AJCHAS; ISSN: 0004-9425

PB CSIRO Publishing

DT Journal

LA English

GI



AB For the syntheses of radiolabeled pyrrolo[1,4]benzodiazepine antitumor antibiotics a method was required to introduce the unstable carbinolamine functionality prior to the radiolabel. In turn, this required the selective redn. of a secondary amide in the presence of a tertiary amide. Methods that can be used to achieve these outcomes were demonstrated in a series of 1H-pyrrolo[2,1-c][1,4]benzodiazepine-5,11-diones. Thus, LiAlH<sub>4</sub> redn. of the (methoxymethyl)pyrrolobenzodiazepinedione I at -60.degree. gave the stannyl imine II in 49% yield, and NaBH<sub>4</sub> redn. of the (tert-butoxycarbonyl) dilactam III (X = O) in EtOH at 0.degree. gave III (X = HO, H) in 42% yield.

IT **187083-49-4P 225784-00-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)

(selective redn. of secondary amide in pyrrolobenzodiazepinediones to carbinolamines)

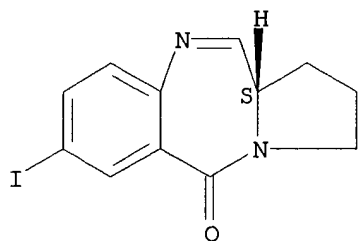
RN 187083-49-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-iodo-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



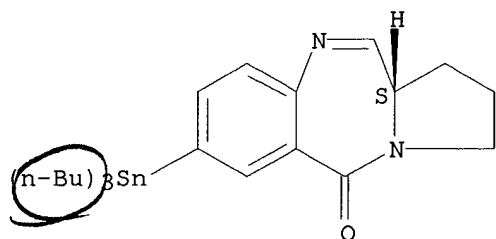
09/763,767



RN 225784-00-9 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(tributylstannyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 39

RE

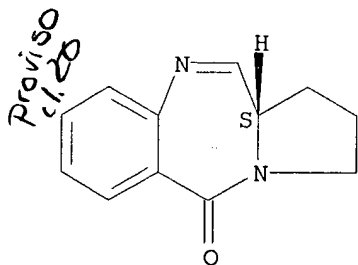
- (2) Barkley, M; Biochemistry 1986, V25, P3021 CAPLUS
- (3) Behling, J; Tetrahedron Lett 1989, V30, P27 CAPLUS
- (4) Farina, V; J Org Chem 1991, V56, P4985 CAPLUS
- (5) Flanagan, R; Appl Radiat Isot 1986, V37, P893 CAPLUS
- (6) Foster, N; J Radioanal Chem 1981, V65, P95 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/763,767

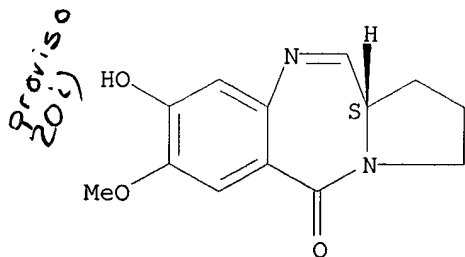
126 ANSWER 15 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1999:108425 CAPLUS  
DN 130:209532  
TI A facile and efficient synthesis of pyrrolo[2,1-c][1,4]benzodiazepine  
antitumor antibiotics: an improved deprotective cyclization method by  
"clayon"  
AU Reddy, B. S. Praveen; Damayanthi, Yalamati; Lown, J. William  
CS Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2,  
Can.  
SO Heterocycl. Commun. (1998), 4(6), 497-500  
CODEN: HCOMEX; ISSN: 0793-0283  
PB Freund Publishing House Ltd.  
DT Journal  
LA English  
OS CASREACT 130:209532  
AB A facile procedure for the prepn. of pyrrolo[2,1-  
c][1,4]benzodiazepine(PBD) imines via ethanethiol deprotective cyclization  
by using a mild and efficient clay supported ammonium nitrate catalyst is  
described. A significant improvement in yield over the customary  
HgCl<sub>2</sub>/HgO deprotective cyclization method is obsd. and the reaction  
proceeds with no detectable racemization.  
IT **72435-89-3P 81307-24-6P 127810-79-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antitumor antibiotics  
using clay supported ammonium nitrate catalyst)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

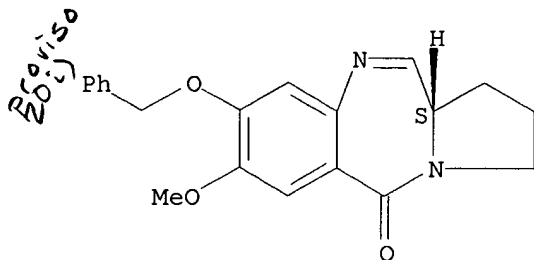


09/763,767

RN 127810-79-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RE.CNT 14

RE

(1) Hurley, L; Nature (London) 1979, V282, P529 CAPLUS

(2) Kamal, A; Bioorg Med Chem Lett 1997, V7, P1825 CAPLUS

(3) Kamal, A; Chem Commun 1996, P385 CAPLUS

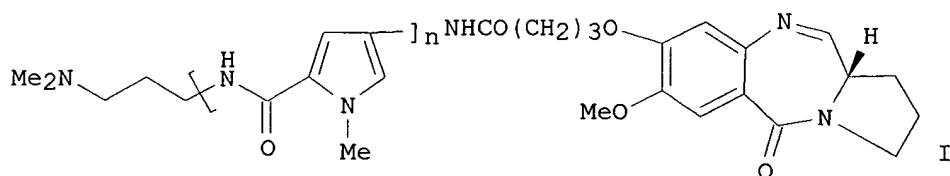
(4) Kamal, A; Chem Commun 1997, P1015 CAPLUS

(5) Kamal, A; Tetrahedron 1997, V53, P3223 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

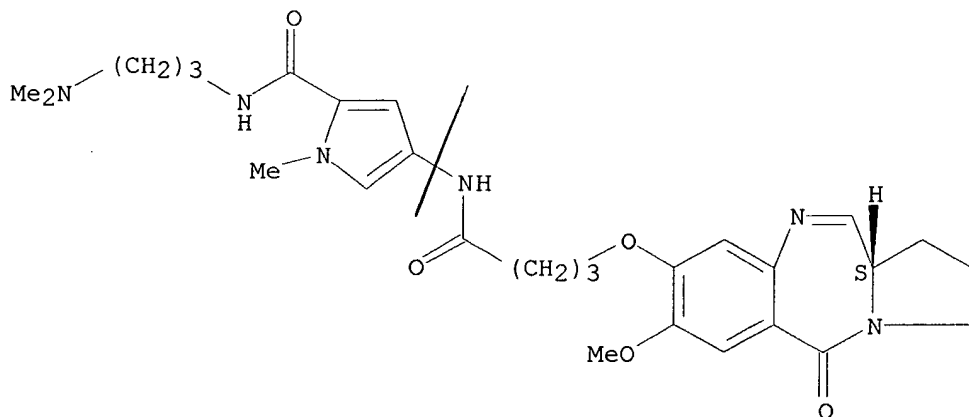
09/763,767

~~126~~ ANSWER 16 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1998:777202 CAPLUS  
DN 130:125384  
TI Design and Synthesis of Novel Pyrrolo[2,1-c][1,4]benzodiazepine-  
Lexitropsin Conjugates  
AU Damayanthi, Yalamati; Reddy, B. S. Praveen; Lown, J. William  
CS Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2G2,  
Can.  
SO J. Org. Chem. (1999), 64(1), 290-292  
CODEN: JOCEAH; ISSN: 0022-3263  
PB American Chemical Society  
DT Journal  
LA English  
OS CASREACT 130:125384  
GI



AB A versatile and convenient strategy for the design and synthesis of a series of novel pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-lexitropsin conjugates I (n = 1-3) bonded through the C8 position with a suitable linker of three carbons (overall five-atom spacer) is described. I were designed in order to examine the combined effect of both moieties on DNA sequence selective binding ability and cytotoxicity (no data).  
IT **219931-74-5P 219931-75-6P 219931-76-7P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(design and synthesis of pyrrolobenzodiazepine-lexitropsin conjugates)  
RN 219931-74-5 CAPLUS  
CN 1H-Pyrrole-2-carboxamide, N-[3-(dimethylamino)propyl]-1-methyl-4-[[[1-oxo-4-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]butyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



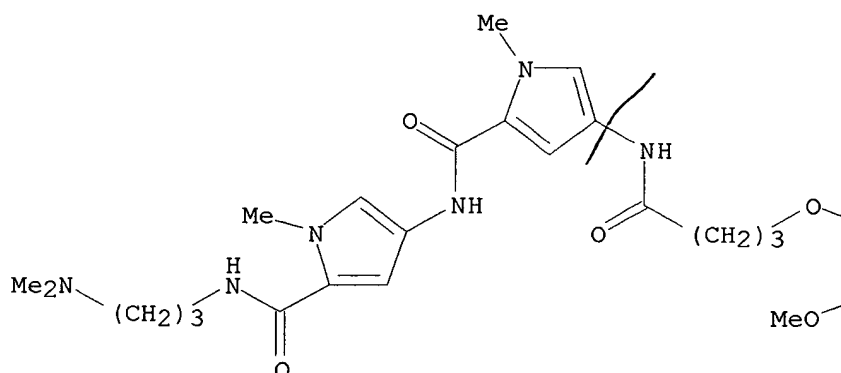
09/763,767

RN 219931-75-6 CAPLUS

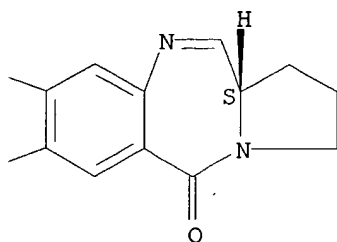
CN 1H-Pyrrole-2-carboxamide, N-[5-[[[3-(dimethylamino)propyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl-4-[[[1-oxo-4-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]butyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

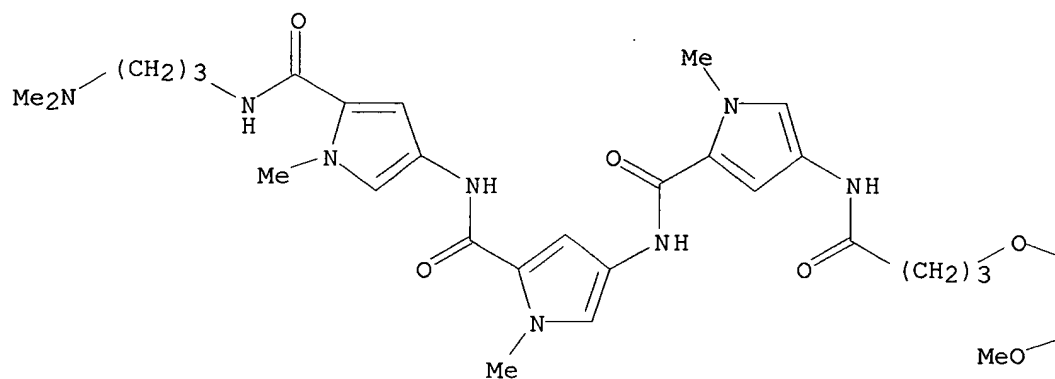


RN 219931-76-7 CAPLUS

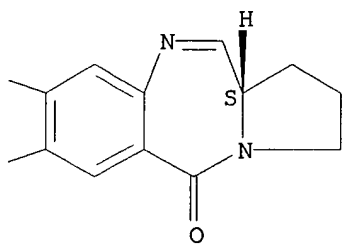
CN 1H-Pyrrole-2-carboxamide, N-[5-[[[3-(dimethylamino)propyl]amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl-4-[[[1-methyl-4-[[[1-oxo-4-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]butyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



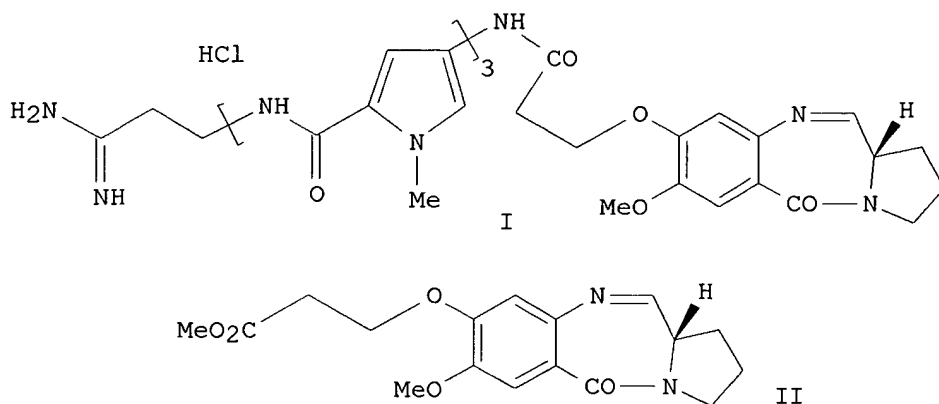
RE.CNT 35

RE

- (1) Bose, D; J Am Chem Soc 1992, V114, P4939 CAPLUS
  - (2) Bose, D; J Chem Soc Chem Commun 1992, P1518 CAPLUS
  - (3) Cheatham, S; J Med Chem 1988, V31, P583 CAPLUS
  - (6) Farmer, J; Tetrahedron Lett 1988, V29, P5105 CAPLUS
  - (7) Fontana, M; Anti-Cancer Drug Design 1992, V7, P131 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/763,767

~~L26~~ ANSWER 17 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1998:760824 CAPLUS  
DN 130:95405  
TI Design, synthesis and biological activity of a pyrrolo[2,1-  
c][1,4]benzodiazepine (PBD)-distamycin hybrid  
AU Baraldi, Pier Giovanni; Cacciari, Barbara; Guiotto, Andrea; Leoni,  
Alberto; Romagnoli, Romeo; Spalluto, Giampiero; Mongelli, Nicola; Howard,  
Philip W.; Thurston, David E.; Bianchi, Nicoletta; Gambari, Roberto  
CS Dipartimento di Scienze Farmaceutiche, Universita di Ferrara, Ferrara,  
44100, Italy  
SO Bioorg. Med. Chem. Lett. (1998), 8(21), 3019-3024  
CODEN: BMCLE8; ISSN: 0960-894X  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
OS CASREACT 130:95405  
GI

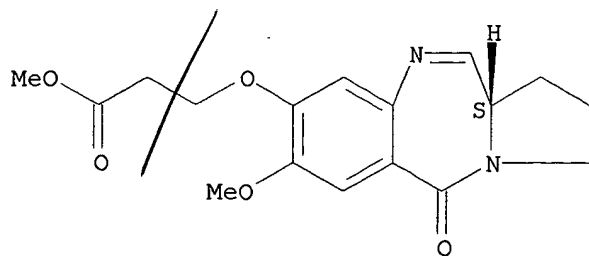


AB The authors report the synthesis of a new hybrid (I) which is a combination of the naturally occurring antitumor agent distamycin A and the pyrrolo[2,1-c][1,4]benzodiazepine (II), related to naturally occurring anthramycin. The antitumor activity of the hybrid I was tested in vitro and compared to the natural product distamycin A and the PBD II.

IT **219562-69-3P 219562-82-0P**  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(design, synthesis and biol. activity of a pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-distamycin hybrid)

RN 219562-69-3 CAPLUS  
CN Propanoic acid, 3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

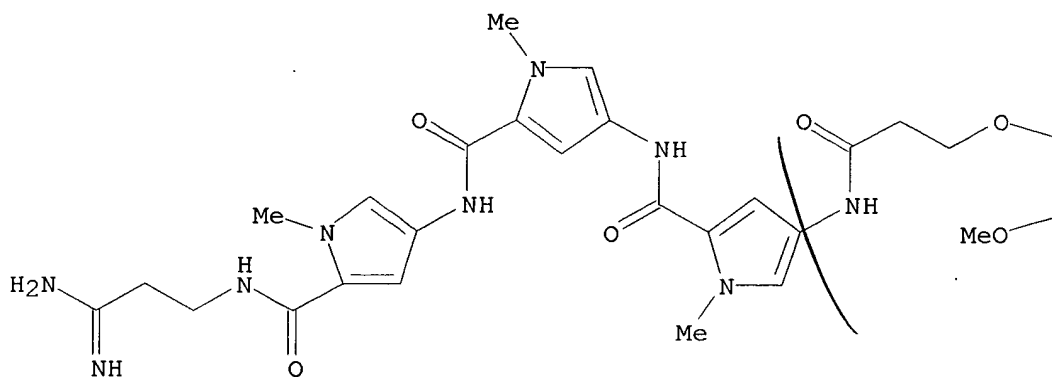


RN 219562-82-0 CAPLUS

CN 1H-Pyrrole-2-carboxamide, N-[5-[[[(3-amino-3-iminopropyl)amino]carbonyl]-1-methyl-1H-pyrrol-3-yl]-1-methyl-4-[[[1-methyl-4-[[1-oxo-3-[[[(11aS)-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl]oxy]propyl]amino]-1H-pyrrol-2-yl]carbonyl]amino]-, monohydrochloride (9CI) (CA INDEX NAME)

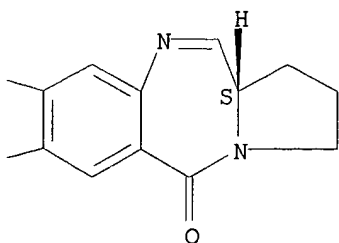
Absolute stereochemistry. Rotation (-).

PAGE 1-A



● HCl

PAGE 1-B





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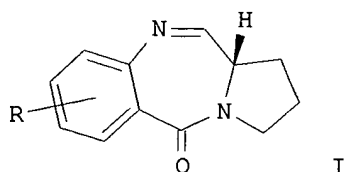
RE.CNT 21

RE

- (1) Arcamone, F; Gazz Chim Ital 1967, V97, P1097 CAPLUS
  - (2) Arcamone, F; Gazzetta Chim Ital 1969, V99, P632 CAPLUS
  - (3) Bianchi, N; Biochem Pharmacol 1996, V52, P1489 CAPLUS
  - (4) Bianchi, N; J Steroid Biochem Molec Biol 1995, V54, P211 CAPLUS
  - (5) Del Senno, L; Human Molec Genetics 1992, V1, P354 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

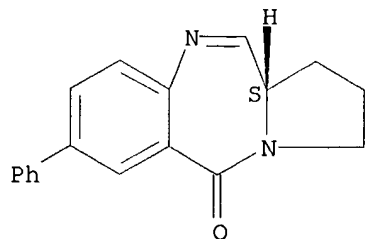
09/763,767

~~L26~~ ANSWER 18 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1998:760823 CAPLUS  
DN 130:95540  
TI Synthesis of novel C7-aryl substituted pyrrolo[2,1-c][1,4]benzodiazepines  
(PBDs) via pro-N10-Troc protection and Suzuki coupling  
AU Guiotto, Andrea; Howard, Philip W.; Baraldi, Pier Giovanni; Thurston,  
David E.  
CS CRC Gene Targeted Drug Design Research Group, School of Pharmacy and  
Biomedical Sciences, University of Portsmouth, Portsmouth, PO1 2DT, UK  
SO Bioorg. Med. Chem. Lett. (1998), 8(21), 3017-3018  
CODEN: BMCLE8; ISSN: 0960-894X  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
OS CASREACT 130:95540  
GI



AB Novel C7-aryl pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) I (R1 = H, 4'-Me, 3'-NO2, etc.) have been synthesized via Suzuki coupling between a 7-Iodo N10-Troc-protected PBD carbinolamine and com. available boronic acids R'C6H4B(OH)2.  
IT **215723-10-7P 219537-15-2P 219537-16-3P**  
**219537-17-4P 219537-18-5P 219537-19-6P**  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and cytotoxicity of aryl pyrrolobenzodiazepines via Suzuki coupling)  
RN 215723-10-7 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-phenyl-, (11aS)- (9CI) (CA INDEX NAME)

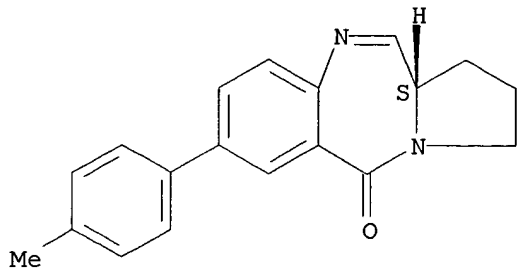
Absolute stereochemistry.



RN 219537-15-2 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(4-methylphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

09/763,767

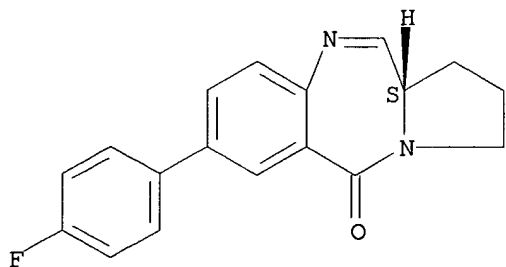
Absolute stereochemistry.



RN 219537-16-3 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-(4-fluorophenyl)-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

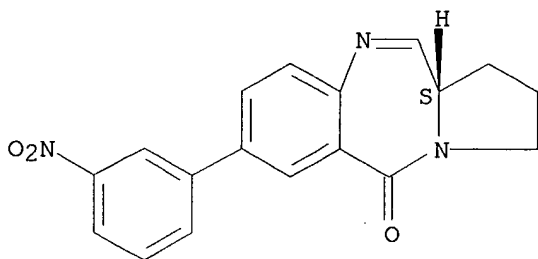
Absolute stereochemistry.



RN 219537-17-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(3-nitrophenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

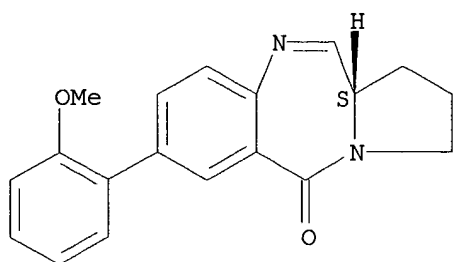


RN 219537-18-5 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(2-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

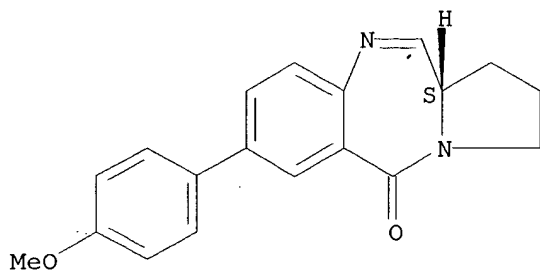
09/763,767



RN 219537-19-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(4-methoxyphenyl)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 7

RE

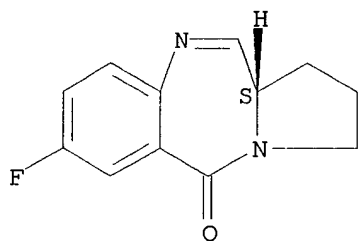
- (1) Dong, Q; Tetrahedron Lett 1995, V36, P5681 CAPLUS
- (2) Miyaura, N; Chem Rev 1995, V95, P2457 CAPLUS
- (3) Puvvada, M; Biochemistry 1997, V36, P2478 CAPLUS
- (4) Puvvada, M; Nucleic Acids Res 1993, V21, P3671 CAPLUS
- (5) Thurston, D; Chem Rev 1994, V94, P433 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

09/763,767

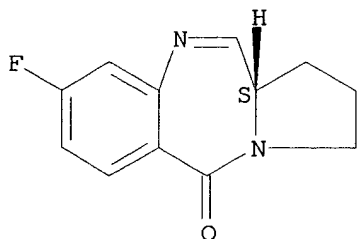
~~LN~~ 6 ANSWER 19 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1998:656968 CAPLUS  
DN 130:3493  
TI DPPE: a convenient replacement for triphenylphosphine in the Staudinger and Mitsunobu reactions  
AU O'Neil, Ian A.; Thompson, Stephen; Murray, Clare L.; Kalindjian, S. Barret  
CS Dep. Chem., Univ. Liverpool, Liverpool, L69 7ZD, UK  
SO Tetrahedron Lett. (1998), 39(42), 7787-7790  
CODEN: TELEAY; ISSN: 0040-4039  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
OS CASREACT 130:3493  
AB DPPE has been shown to replace triphenylphosphine in the Staudinger and Mitsunobu reactions. The resulting bis(phosphine oxide) byproduct is readily removed allowing for rapid and simple purifn. of the reaction mixt.  
IT **215723-03-8P 215723-04-9P 215723-05-0P**  
**215723-06-1P 215723-07-2P 215723-08-3P**  
**215723-09-4P 215723-10-7P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(use of DPPE in the Staudinger and Mitsunobu reactions)  
RN 215723-03-8 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-fluoro-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 215723-04-9 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8-fluoro-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

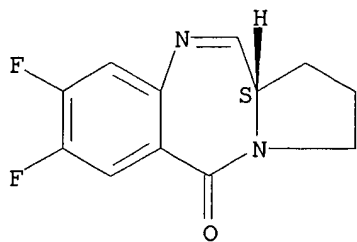


RN 215723-05-0 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,8-difluoro-1,2,3,11a-

09/763,767

tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

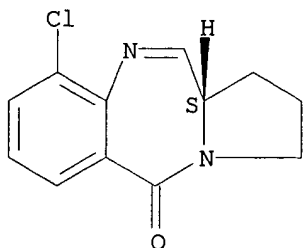
Absolute stereochemistry.



RN 215723-06-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-chloro-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

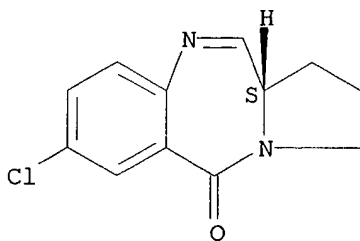
Absolute stereochemistry.



RN 215723-07-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-chloro-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

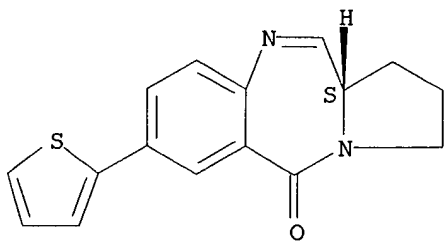


RN 215723-08-3 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-(2-thienyl)-, (11aS)- (9CI) (CA INDEX NAME)

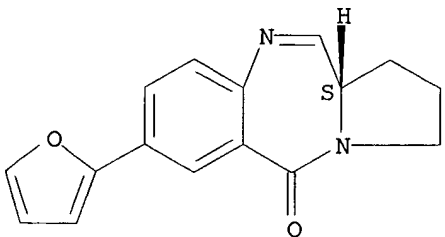
Absolute stereochemistry.

09/763,767



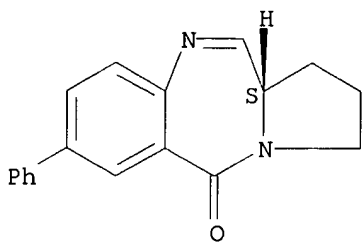
RN 215723-09-4 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-(2-furanyl)-1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 215723-10-7 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-phenyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



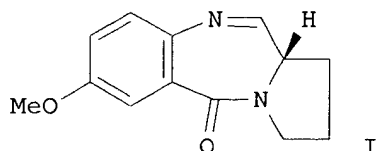
RE.CNT 15

RE

- (1) Amos, R; J Org Chem 1983, V48, P3598 CAPLUS
  - (2) Camp, D; Aust J Chem 1988, V41, P1835 CAPLUS
  - (3) Castro, R; J Org Chem 1996, V61, P7298 CAPLUS
  - (4) Eguchi, S; J Org Chem 1995, V60, P4006 CAPLUS
  - (5) Etter, M; J Am Chem Soc 1988, V110, P639 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

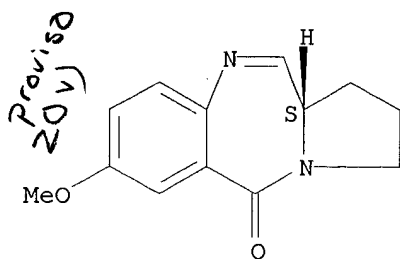
09/163,767

~~LN~~6 ANSWER 20 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1998:617896 CAPLUS  
DN 129:302623  
TI Synthesis of pyrrolobenzodiazepines via the PIFA oxidation of amines.  
Synthesis of 8-deoxy DC-81  
AU Kraus, George A.; Melekhov, Alex  
CS Department of Chemistry, Iowa State University, Ames, IA, 50011, USA  
SO Tetrahedron (1998), 54(39), 11749-11754  
CODEN: TETRAB; ISSN: 0040-4020  
PB Elsevier Science Ltd.  
DT Journal  
LA English  
GI



AB Bis(trifluoroacetoxy)iodobenzene (PIFA) can be used to introduce the imine moiety into a precursor to the pyrrolobenzodiazepines in 62% yield. This oxidn. completes an efficient four-step synthesis of 8-deoxy DC-81 (I).  
IT **133954-34-4P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(pyrrolobenzodiazepines via PIFA oxidn. of amines)  
RN 133954-34-4 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

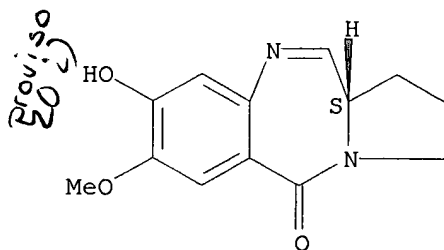
Absolute stereochemistry.





~~LA~~ 6 ANSWER 21 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1998:461819 CAPLUS  
 DN 129:188890  
 TI A mild and facile reduction of azides to amines by N,N-dimethylhydrazine and catalytic ferric chloride  
 AU Kamal, Ahmed; Reddy, B. S. Narayan  
 CS Division of Organic Chemistry, Indian Institute of Chemical Technology, Hyderabad, 500 007, India  
 SO Chem. Lett. (1998), (7), 593-594  
 CODEN: CMLTAG; ISSN: 0366-7022  
 PB Chemical Society of Japan  
 DT Journal  
 LA English  
 OS CASREACT 129:188890  
 AB Reaction of a variety of azido compds. with N,N-dimethylhydrazine in the presence of a catalytic amt. of ferric chloride hexahydrate in methanol results in excellent yields of the corresponding amino compds. This reductive system is compatible with a wide assortment of functional groups and has also been extended towards the synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics. The redn. and cyclization of (S)-1-(2-azido-4-hydroxy-5-methoxybenzoyl)-2-pyrrolidinecarboxaldehyde gave Antibiotic DC 81 [i.e., (1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy)-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one].  
 IT **81307-24-6P**, Antibiotic DC 81  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 81307-24-6 CAPLUS  
 CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

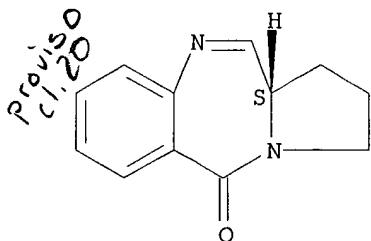
Absolute stereochemistry.



09/763,767

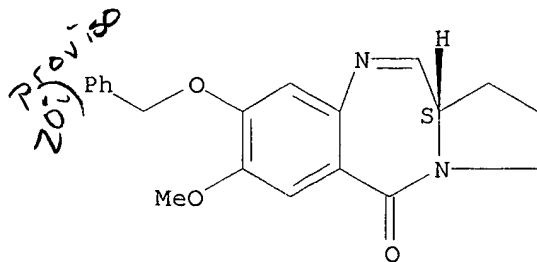
~~126~~ ANSWER 22 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1998:66432 CAPLUS  
DN 128:154068  
TI A new methodology for the reductive cyclization of .omega.-azido carbonyl compounds mediated by tetrathiomolybdate. Application to an efficient synthesis of pyrrolo[2,1-c][1,4]benzodiazepines  
AU Prabhu, Kandikere R.; Sivanand, P. S.; Chandrasekaran, Srinivasan  
CS Department Organic Chemistry, Indian Institute Science, Bangalore, 560012, India  
SO Synlett (1998), (1), 47-48  
CODEN: SYNLES; ISSN: 0936-5214  
PB Georg Thieme Verlag  
DT Journal  
LA English  
OS CASREACT 128:154068  
AB The .omega.-azido carbonyl compds. on treatment with [PhCH<sub>2</sub>NEt<sub>3</sub>]<sub>2</sub>MoS<sub>4</sub> led to the formation of 5-, 6-, and 7-membered cyclic imines in very good yields under mild conditions. This method is applied successfully to an efficient synthesis of 1,4-benzodiazepinones and in particular benzylated DC-81.  
IT **72435-89-3P 127810-79-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of pyrrolobenzodiazepines by thiomolybdate-mediated reductive cyclization of .omega.-azido carbonyl compds.)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



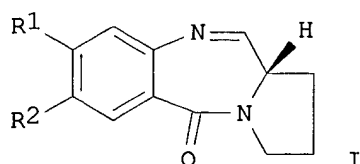
RN 127810-79-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



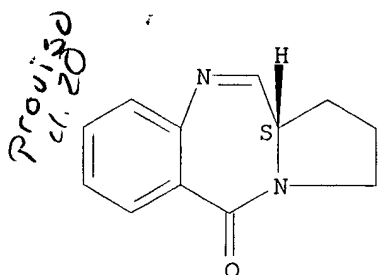
09/763,767

~~DI~~ 6 ANSWER 23 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1997:538783 CAPLUS  
DN 127:220632  
TI An efficient synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics  
via reductive cyclization  
AU Kamal, Ahmed; Reddy, B. S. Nararyan; Reddy, B. S. Praveen  
CS Division of Organic Chemistry, Indian Institute of Chemical Technology,  
Hyderabad, 500 007, India  
SO Bioorg. Med. Chem. Lett. (1997), 7(14), 1825-1828  
CODEN: BMCLE8; ISSN: 0960-894X  
PB Elsevier  
DT Journal  
LA English  
OS CASREACT 127:220632  
GI



AB A new and convenient one-pot synthesis of pyrrolo[2,1-c][1,4]benzodiazepines (PBD) (I; R1 = R2 = H; R1 = OCH2Ph, R2 = OMe; R1 = OH, R2 = OMe) has been achieved by a reductive cyclization employing N,N-dimethylhydrazine and FeCl3.6H2O in good yields.  
IT **72435-89-3P 81307-24-6P 127810-79-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of pyrrolbenzodiazepines by reductive cyclization)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

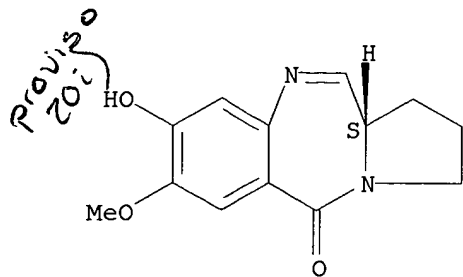
Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

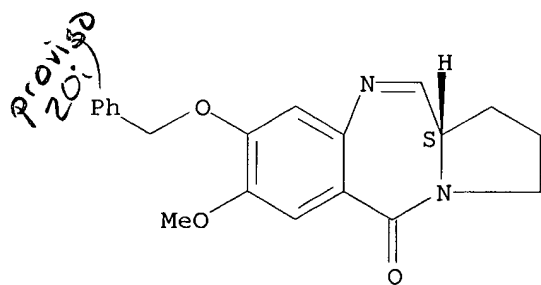
09/763,767



RN 127810-79-1 CAPLUS

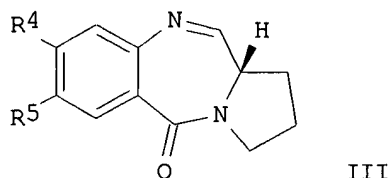
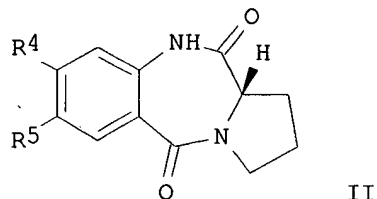
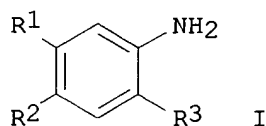
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



09/763,767

DI 6 ANSWER 24 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1997:403325 CAPLUS  
DN 127:81265  
TI Novel biocatalytic reduction of aryl azides: chemoenzymic synthesis of  
pyrrolo[2,1-c][1,4]benzodiazepine antibiotics  
AU Kamal, Ahmed; Damayanthi, Y.; Reddy, B. S. Narayan; Lakminarayana, B.;  
Reddy, B. S. Praveen  
CS Indian Inst. Chem. Technol., Hyderabad, 500 007, India  
SO Chem. Commun. (Cambridge) (1997), (11), 1015-1016  
CODEN: CHCOFS; ISSN: 1359-7345  
PB Royal Society of Chemistry  
DT Journal  
LA English  
OS CASREACT 127:81265  
GI

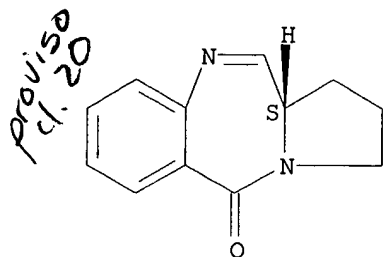


AB The chemoselective redn. of aryl azides to aryl amines (I) (R<sub>1</sub> = H, Me; R<sub>2</sub> = H, Cl, F, OMe; R<sub>3</sub> = H, CO<sub>2</sub>H, OH), and the synthesis of the imine-contg. pyrrolo[2,1-c][1,4]benzodiazepine DNA-binding antitumor antibiotics (II) and (III) (R<sub>4</sub> = H, OH, OCH<sub>2</sub>Ph; R<sub>5</sub> = Me, OMe) by selective biocatalytic reductive cyclization of azido aldehydes, has been achieved by employing baker's yeast.  
IT 72435-89-3P 81307-24-6P 127810-79-1P  
182508-34-5P  
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)  
(chemoenzymic synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via biocatalytic redn. of aryl azides)  
RN 72435-89-3 CAPLUS

09/763,767

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

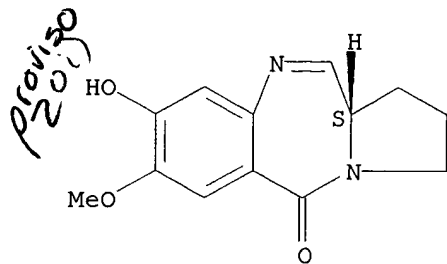
Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

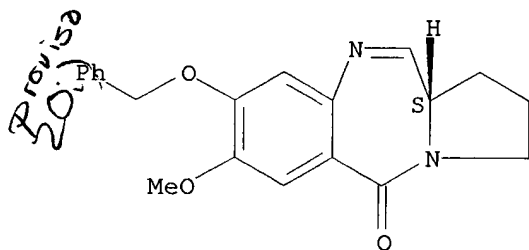
Absolute stereochemistry.



RN 127810-79-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-  
8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

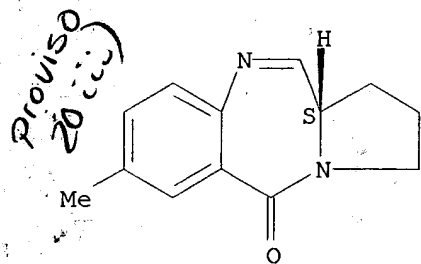


RN 182508-34-5 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl-,  
(11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

09/763,767



09/763,767

~~DI~~ 6 ANSWER 25 OF 107 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1997:349351 CAPLUS

~~DN~~ 127:81431

TI The synthesis of a novel benzodiazocine via an intramolecular Staudinger/aza-Wittig cyclization

AU O'neil, Ian A.; Murray, Clare L.; Potter, Andrew J.; Kalindjian, S. Barret

CS Department of Chemistry, University of Liverpool, Liverpool, L69 3BX, UK

SO Tetrahedron Lett. (1997), 38(20), 3609-3610

CODEN: TELEAY; ISSN: 0040-4039

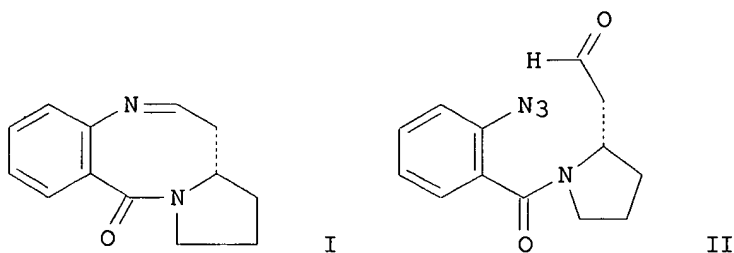
PB Elsevier

DT Journal

LA English

OS CASREACT 127:81431

GI



AB The novel pyrrolobenzodiazocine I has been prepd. by an intramol. Staudinger/aza Wittig protocol from the precursor azido aldehyde II in a remarkable 93% yield. Aldehyde II was prepd. by coupling protected homoprolinol with 2-azidobenzoic acid followed by deprotection and oxidn.

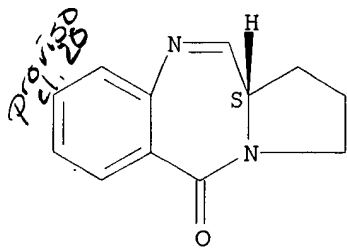
IT **72435-89-3P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of benzodiazocine via Staudinger-aza-Wittig cyclization)

RN 72435-89-3 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

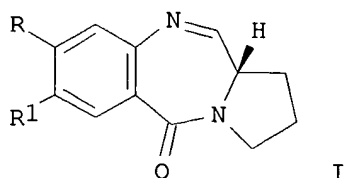
Absolute stereochemistry. Rotation (+).





09/763,767

~~L26~~ ANSWER 26 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~RN~~ 1997:165424 CAPLUS  
DN 126:225131  
TI Synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics: oxidation of  
cyclic secondary amine with TPAP  
AU Kamal, Ahmed; Howard, Philip W.; Reddy, B. S. Narayan; Reddy, B. S.  
Praveen; Thurston, David E.  
CS Div. Org. Chem., Indian Inst. Chem. Technol., Hyderabad, 500 007, India  
SO Tetrahedron (1997), 53(9), 3223-3230  
CODEN: TETRAB; ISSN: 0040-4020  
PB Elsevier  
DT Journal  
LA English  
OS CASREACT 126:225131  
GI

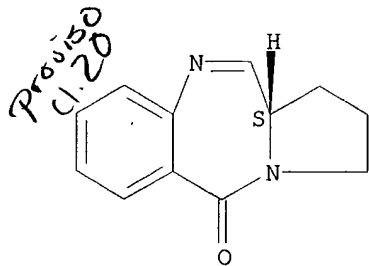


AB A facile procedure for the prepn. of the imine form of the  
pyrrolo[2,1-c][1,4]-benzodiazepine ring system I (R, R1 = H; R = OH, R1 =  
MeO) by the oxidn. of cyclic secondary amine with catalytic amts. of  
tetra-n-propylammonium perruthenate (TPAP) and N-methylmorpholine N-oxide  
(NMO) as a co-oxidant is described. This oxidative method is devoid of  
side-products and is thus a significant improvement over the Swern oxidn.  
previously reported.

IT **72435-89-3P 81307-24-6P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via oxidn.  
of cyclic secondary amine with tetra-n-propylammonium perruthenate)

RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

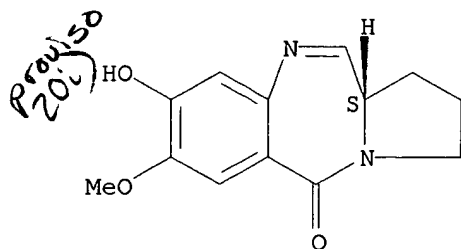
Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

09/763,767

Absolute stereochemistry.



09/763,767

~~LT~~ ANSWER 27 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1997:164900 CAPLUS

DN 126:139567

TI Inhibition of Bacteriophage T7 RNA Polymerase in Vitro Transcription by DNA-Binding Pyrrolo[2,1-c][1,4]benzodiazepines

AU Puvvada, Madhu S.; Forrow, Stephen A.; Hartley, John A.; Stephenson, Pauline; Gibson, Ian; Jenkins, Terence C.; Thurston, David E.

CS Gene Targeted Drug Design Research Group School of Pharmacy and Biomedical Science, University of Portsmouth, Portsmouth, PO1 2DT, UK

SO Biochemistry (1997), 36(9), 2478-2484

CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

AB The interactions of several pyrrolo[2,1-c][1,4]benzodiazepine (PBD) antitumor antibiotics with linearized plasmid p-GEM-2-N-ras DNA have been analyzed by quant. in vitro transcription (QIVT) and in vitro transcription footprinting (IVTF) methods. A concn.-dependent inhibitory effect of the PBDs on transcription is obsd. using both techniques. The rank order for overall inhibition of transcription by the QIVT method is : sibiromycin > tomaymycin > anthramycin > DC-81 > neothramycin, whereas the IVTF expts. show a different ranking: sibiromycin > anthramycin > neothramycin > tomaymycin. In addn., stimulation of transcription was obsd. at low PBD concns. in both the QIVT and IVTF expts. These results demonstrate unequivocally that the formation of PBD-DNA adducts at AGA-5' base sequences on the transcribed strand results in transcription blockage for all PBDs examd. Furthermore, the sequence of flanking base pairs appears to influence the degree of blocking, with the sequences ACAGAAA-5', AAAGATG-5', AGAGATA-5', and CAAGAAC-5' providing the most pronounced blocks for all PBDs in this system. Neothramycin and tomaymycin cause addnl. blocks at some GGA-5' and TGA-5' sequences. Parallel MPE-Fe(II) footprinting studies have revealed PBD binding sites on both the transcribing and nontranscribing strands, although all transcription blocks detd. from the IVTF assays are due to drug bound on the transcribing DNA template strand.

IT 81307-24-6, DC-81

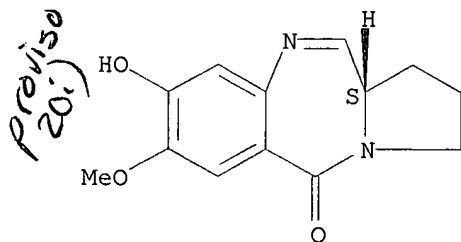
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(inhibition of bacteriophage T7 RNA polymerase in vitro transcription by DNA-binding pyrrolo[c][1,4]benzodiazepines)

RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

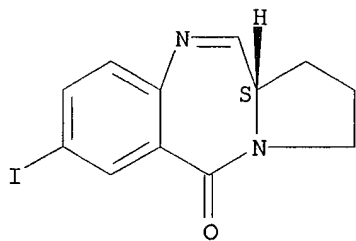
Absolute stereochemistry.



09/763,767

~~D26~~ ANSWER 28 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1997:110812 CAPLUS  
~~DN~~ 126:171573  
TI The synthesis of functionalized pyrrolo[2,1-c][1,4]benzodiazepines  
AU O'Neil, Ian; Murray, Clare L.; Hunter, Rachel C.; Kalindjian, S. Barret;  
Jenkins, Terry C.  
CS Dep. Chem., Univ. Liverpool, Liverpool, L69 3BX, UK  
SO Synlett (1997), (1), 75-78  
CODEN: SYNLES; ISSN: 0936-5214  
PB Thieme  
DT Journal  
LA English  
OS CASREACT 126:171573  
AB Two concise and high yielding routes to the pyrrolo[2,1-c][1,4]benzodiazepine ring system are described. Thus, condensation of prolinol with 2-azidobenzoyl chloride gives the corresponding amide. Oxidn. to the aldehyde followed by generation of the phosphorimine by Staudinger reaction results in ring closure via an aza-Wittig reaction to yield the desired ring system. Alternatively, coupling of prolinol with the appropriate isatoic anhydride yields the corresponding amino alc. Oxidn. with Dess-Martin periodinane yields the title compds. in moderate to good yield. The cytotoxicity of bromo, chloro, and iodo derivs. against human ovarian carcinoma cells was detd. The most active compd. showed IC50 ratios of 0.54 and 1.65.  
IT **187083-49-4P 187083-50-7P 187337-77-5P**  
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and antitumor activity of pyrrolobenzodiazepines)  
RN 187083-49-4 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-iodo-, (11aS)- (9CI) (CA INDEX NAME)

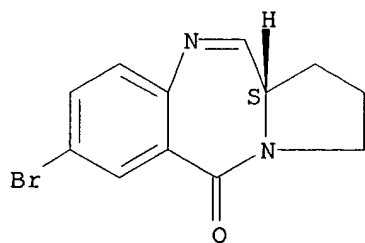
Absolute stereochemistry.



RN 187083-50-7 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-bromo-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

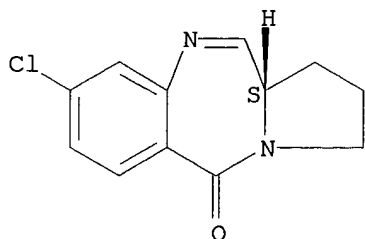
Absolute stereochemistry.

09/763,767



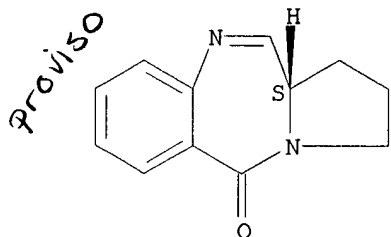
RN 187337-77-5 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8-chloro-1,2,3,11a-tetrahydro-,  
(S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 72435-89-3P 187083-51-8P 187083-52-9P  
187083-53-0P 187083-54-1P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis and antitumor activity of pyrrolobenzodiazepines)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

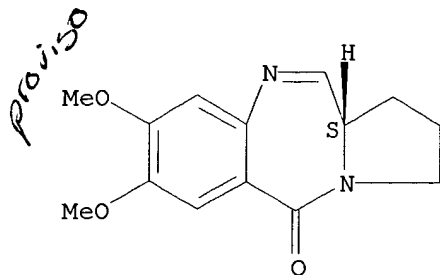
Absolute stereochemistry. Rotation (+).



RN 187083-51-8 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,8-  
dimethoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

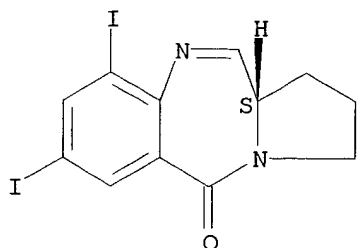
09/763,767



RN 187083-52-9 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7,9-diiodo-, (S)- (9CI) (CA INDEX NAME)

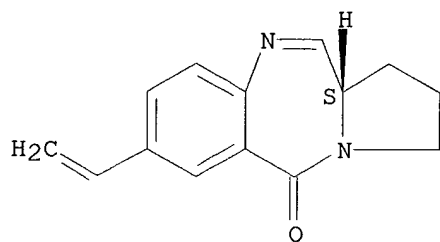
Absolute stereochemistry.



RN 187083-53-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-ethenyl-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

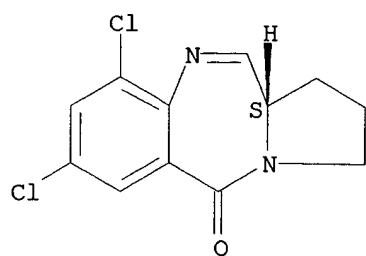


RN 187083-54-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,9-dichloro-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

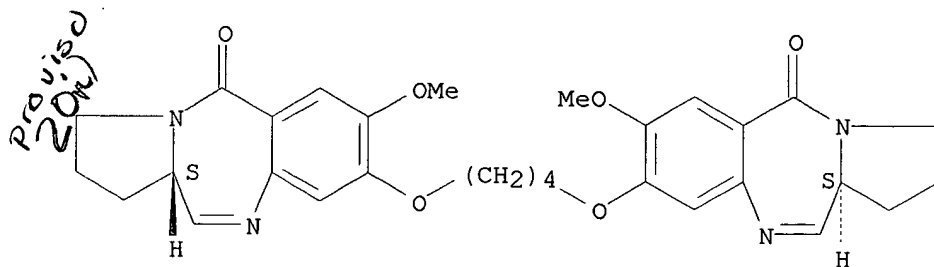
09/763,767



09/763,767

~~L26~~ ANSWER 29 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1996:644058 CAPLUS  
DN 126:8088  
TI Synthesis of Sequence-Selective C8-Linked Pyrrolo[2,1-c][1,4]benzodiazepine Interstrand DNA Crosslinking Agents  
AU Thurston, David E.; Bose, D. Subhas; Thompson, Andrew S.; Howard, Philip W.; Leoni, Alberto; Croker, Stephen J.; Jenkins, Terrence C.; Neidle, Steven; Hartley, John A.; Hurley, Laurence H.  
CS School of Pharmacy and Biomedical Science, University of Portsmouth, Portsmouth/Hants, PO1 2DT, UK  
SO J. Org. Chem. (1996), 61(23), 8141-8147  
CODEN: JOCEAH; ISSN: 0022-3263  
PB American Chemical Society  
DT Journal  
LA English  
AB An efficient convergent synthesis of a homologous series of C8-linked pyrrolobenzodiazepine dimers with remarkable DNA interstrand crosslinking activity and potent in vitro cytotoxicity is reported. The "amino thioacetal" cyclization procedure was used to produce the electrophilic DNA-interactive N10-C11 imine moiety during the final synthetic step. In order to construct the key A-ring fragments, a versatile convergent approach has been developed to join two units of vanillic acid with .alpha.,.omega.-dihaloalkanes of varying length to provide the required bis(4-carboxy-2-methoxyphenoxy)alkanes while avoiding the formation of mixts. of monoalkylated and bisalkylated products.  
IT **145325-56-0P 145325-57-1P 145325-58-2P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 145325-56-0 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,4-butanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

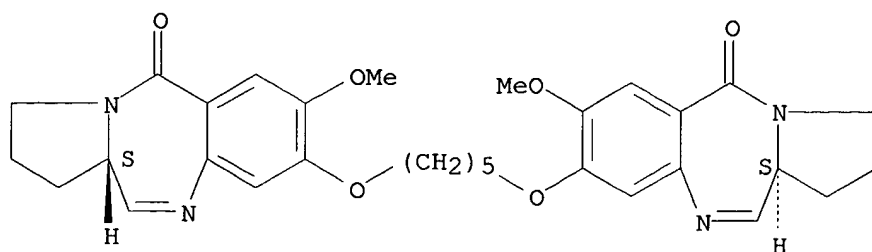


RN 145325-57-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanedylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



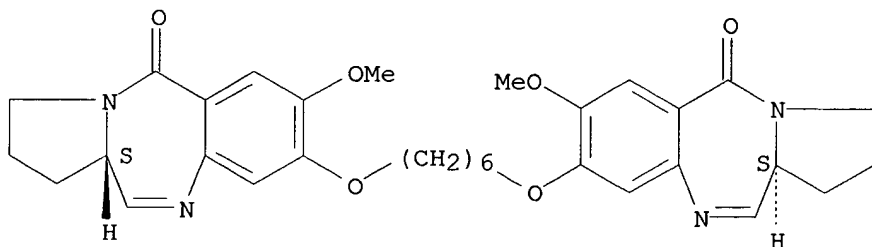
09/763,767



RN 145325-58-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,6-hexanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, [S-(R\*,R\*)]- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



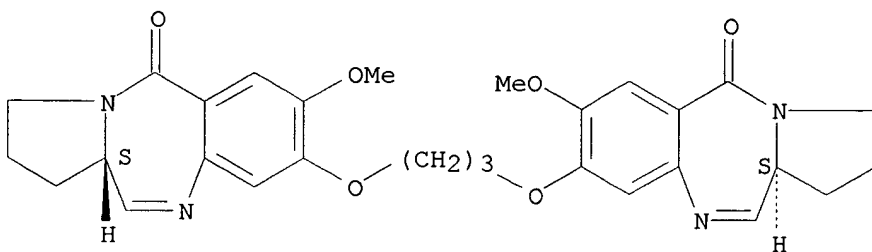
IT **140676-21-7P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of sequence-selective C8-Linked pyrrolobenzodiazepine  
interstrand DNA crosslinking agents)

RN 140676-21-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-  
(9CI) (CA INDEX NAME)

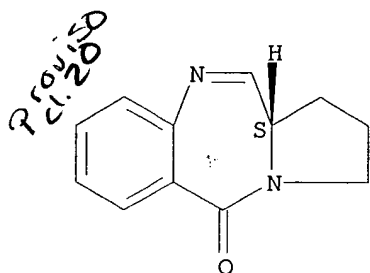
Absolute stereochemistry.



09/763,767

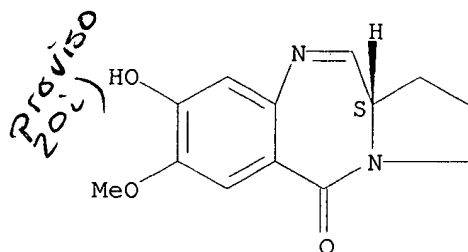
L26 ANSWER 30 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1996:575031 CAPLUS  
DN 125:275482  
TI Synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via azido reductive cyclization with HMDST  
AU Kamal, Ahmed; Reddy, B. S. Praveen; Reddy, B. S. Narayan  
CS Div. Org. Chem., Indian Inst. Chem. Technol., Hyderabad, 500 007, India  
SO Tetrahedron Lett. (1996), 37(37), 6803-6806  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 125:275482  
AB A new facile synthesis of pyrrolo[2,1-c][1,4]benzodiazepine ring system has been achieved by reductive cyclization of azide employing hexamethyldisilathiane (HMDST). The parent unsubstituted ring system and the natural product DC-81 have been prepd. in good overall yields.  
IT **72435-89-3P 81307-24-6P, DC-81 182277-13-0P 182508-34-5P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of pyrrolobenzodiazepines by reductive cyclization of azide with hexamethyldisilathiane)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)-(9CI) (CA INDEX NAME)

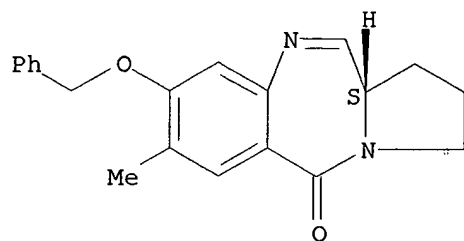
Absolute stereochemistry.



RN 182277-13-0 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl-8-(phenylmethoxy)-, (S)-(9CI) (CA INDEX NAME)

09/763,767

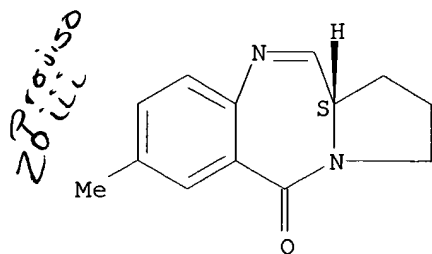
Absolute stereochemistry.



RN 182508-34-5 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl-,  
(11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

126 ANSWER 31 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1996:550992 CAPLUS

IN 125:264974

TI Preclinical pharmacology and antitumor activity of the novel  
sequence-selective DNA minor-groove crosslinking agent DSB-120

AU Walton, M. I.; Goddard, P.; Kelland, L. R.; Thurston, D. E.; Harrap, K. R.  
CS Institute Cancer Research, CRC Center Cancer Therapeutics, Belmont, SM2  
5NG, UK

SO Cancer Chemother. Pharmacol. (1996), 38(5), 431-438  
CODEN: CCPHDZ; ISSN: 0344-5704

DT Journal

LA English

AB In vitro cytotoxicity, antitumor activity, and preclin. pharmacokinetics  
of the novel sequence-selective, bifunctional alkylating agent DSB-120  
(I), a synthetic pyrrolo[1,4][2,1-c]benzodiazepine dimer, was  
investigated. I was shown to be a potent cytotoxic agent against a panel  
of human colon carcinomas and two rodent tumors (L1210 and ADJ/PC6). The  
maximal antitumor effects were obsd. following a single i.v. dose but the  
therapeutic index was only 2.6. I was less effective when given i.p.  
either singly or by a daily x5 schedule. After a single i.v. dose at the  
max. tolerated dose the plasma elimination was biphasic, with a short  
distribution phase being followed by a longer elimination phase. Concns.  
of I in ADJ/PC6 tumors were very low, showing a peak of 0.4 .mu.gg at 5  
min. The steady-state tumor/plasma ratio was about 5% and the AUC was  
only 2.5% of that occurring in the plasma. I appeared to be unstable in  
vivo, with only 1% of an administered dose being recovered unchanged in 24  
h urine samples. Plasma protein binding was extensive at 96.6%. In  
conclusion, the poor antitumor activity of ,I may be a consequence of low  
tumor selectivity and drug uptake as a result of protein binding and/or  
extensive drug metab in vivo.

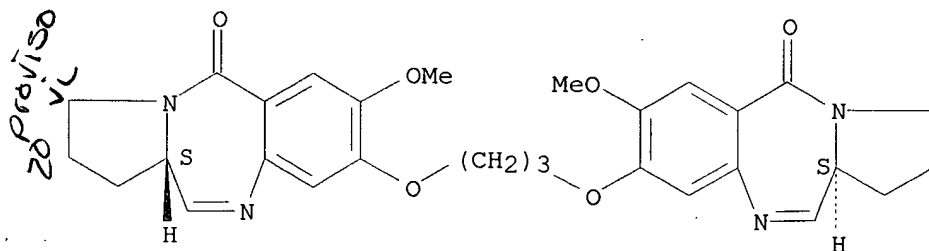
IT 140676-21-7

RL: BPR (Biological process); THU (Therapeutic use); BIOL (Biological  
study); PROC (Process); USES (Uses)  
(preclin. pharmacol. and antitumor activity of DNA minor-groove  
crosslinking agent DSB-120)

RN 140676-21-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-  
propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-  
(9CI) (CA INDEX NAME)

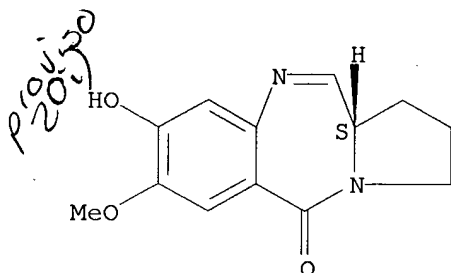
Absolute stereochemistry.



09/763,767

~~126~~ ANSWER 32 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN- 1996:490671 CAPLUS  
DN 125:184902  
TI Molecular mechanics study of the stereochemistry of formation of covalent  
pyrrolobenzodiazepine-DNA adducts  
AU Adams, L. J.; Morris, S. J.; Banting, L.; Jenkins, T. C.; Thurston, D. E.  
CS Cent. Molecular Design, Univ. Portsmouth, Portsmouth, PO1 2ED, UK  
SO Pharm. Sci. (1995), 1(3), 151-154  
CODEN: PHSCFB; ISSN: 1356-6881  
DT Journal  
LA English  
AB The pyrrolobenzodiazepine (PBD) antitumor antibiotics are known to react  
at their C11-position with a no. of different nucleophiles, including DNA,  
to give a predominance of either C11(R) or C11(S) adducts, depending upon  
structural features such as the degree of satn. of the C-ring. This  
behavior has now been rationalized on the basis of mol. mechanics calcns.  
IT **81307-24-6**, DC-81  
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study);  
PROC (Process)  
(mol. mechanics study of stereochem. of formation of covalent  
pyrrolobenzodiazepine-DNA adducts)  
RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

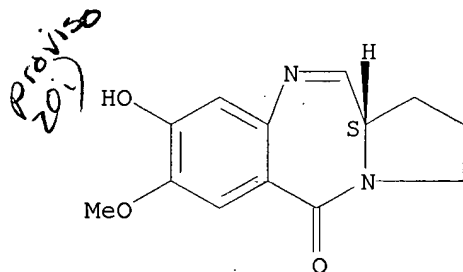
Absolute stereochemistry.



09/763,767

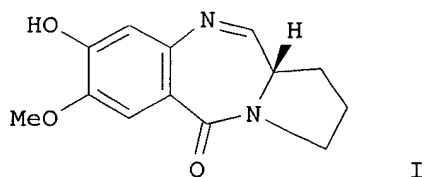
~~LX~~ 6 ANSWER 33 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1996:380978 CAPLUS  
DN 125:104253  
TI DNA-binding properties of pyrrolo[2,1-c][1,4]benzodiazepine N10-C11  
amidines  
AU Foloppe, M. P.; Rault, S.; Thurston, D. E.; Jenkins, T. C.; Robba, M.  
CS Cent. Etud. Rech. Medicament Normandie, Caen, 14032, Fr.  
SO Eur. J. Med. Chem. (1996), 31(5), 407-410  
CODEN: EJMCA5; ISSN: 0223-5234  
DT Journal  
LA English  
AB A series of pyrrolo[2,1-c][1,4]benzodiazepine N10-C11 amidines has been  
evaluated for in vitro DNA binding through thermal denaturation studies.  
Some of these compds. cause a significant increase in melting for calf  
thymus DNA (e.g., 0.7+-.0.1.degree.), possibly due to non-covalent  
interaction with bases positioned on the floor of the minor groove in the  
DNA duplex.  
IT **81307-24-6**, DC-81  
RL: BAC (Biological activity or effector, except adverse); PRP  
(Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(DNA-binding properties of pyrrolo[2,1-c][1,4]benzodiazepine N10-C11  
amidines)  
RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

126 ANSWER 34 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1996:198494 CAPLUS  
DN 124:316822  
TI A new facile procedure for the preparation of pyrrolo[2,1-c][1,4]benzodiazepines: synthesis of the antibiotic DC-81 and its thio analog  
AU Kamal, Ahmed; Reddy, B. S. Praveen; Reddy, B. S. Narayan  
CS Div. Org. Chem., Indian Inst. Chem. Technol., Hyderabad, 500 007, India  
SO Tetrahedron Lett. (1996), 37(13), 2281-4  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 124:316822  
GI

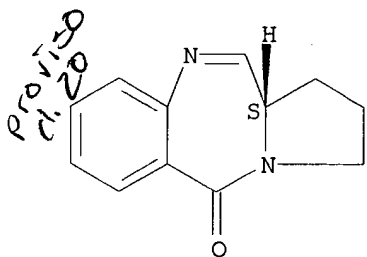


AB An efficient synthesis of the imine form of the pyrrolo[2,1-c][1,4]benzodiazepine ring system based on a new reductive cyclization procedure is described. The naturally occurring antibiotic DC-81 (I) and its 5-thio analog have also been synthesized to illustrate the usefulness of this methodol.

IT **72435-89-3P 81307-24-6P**, Antibiotic dc 81  
**127810-79-1P 175521-32-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of pyrrolo[2,1-c][1,4]benzodiazepines)

RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-(9CI) (CA INDEX NAME)

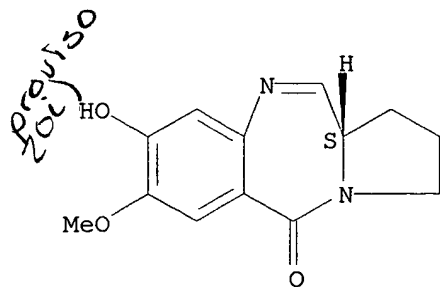
Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

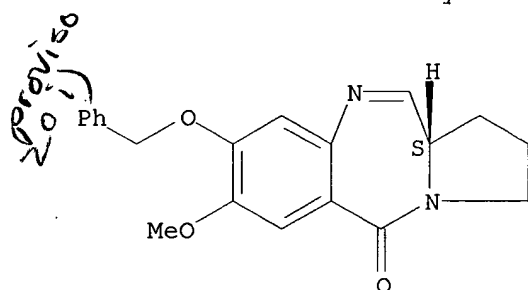
09/763,767



RN 127810-79-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

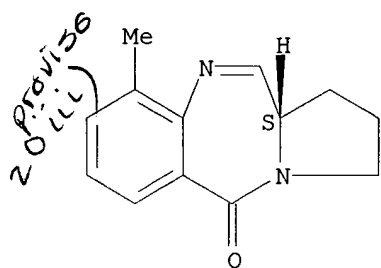
Absolute stereochemistry. Rotation (+).



RN 175521-32-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methyl-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

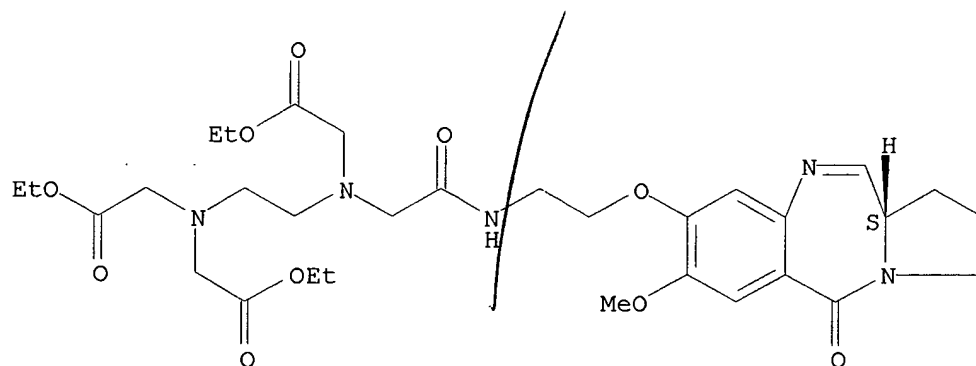




09/763,767

~~L26~~ ANSWER 35 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1996:158919 CAPLUS  
DN 124:283579  
TI Synthesis of a novel GC-specific covalent-binding DNA affinity-cleavage agent based on pyrrolobenzodiazepines (PDBs)  
AU Thurston, David E.; Morris, Steven J.; Hartley, John A.  
CS Sch. Pharmacy Biomedical Science, Univ. Portsmouth, Portsmouth, PO1 2DZ, UK  
SO Chem. Commun. (Cambridge) (1996), (4), 563-5  
CODEN: CHCOFS; ISSN: 1359-7345  
DT Journal  
LA English  
AB Reported is the attachment of an EDTA moiety to DC-81, a member of the guanine(N2)-specific pyrrolobenzodiazepine family of antitumor antibiotics, to produce the first example of a covalent-binding GC-specific DNA-cleaving agent with a selectivity for 5'-PuG Pu sequences (Pu = purine; G = guanine).  
IT **175733-07-0P 175733-08-1DP**, iron complexes  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of GC-specific covalent-binding DNA affinity-cleavage agent based on pyrrolobenzodiazepines)  
RN 175733-07-0 CAPLUS  
CN Glycine, N-[2-[bis(2-ethoxy-2-oxoethyl)amino]ethyl]-N-[2-oxo-2-[[2-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]ethyl]amino]ethyl]-, ethyl ester, (S)- (9CI) (CA INDEX NAME)

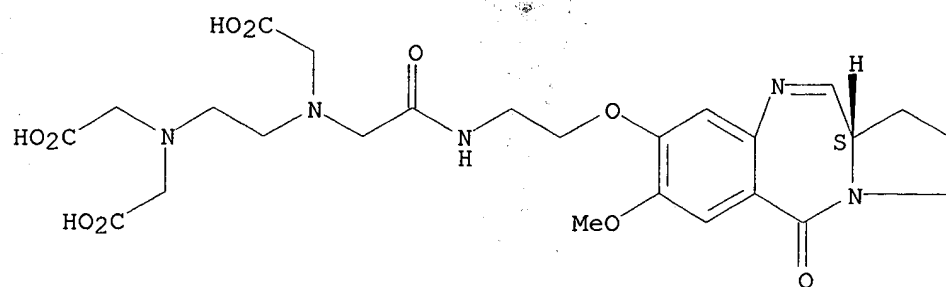
Absolute stereochemistry.



RN 175733-08-1 CAPLUS  
CN Glycine, N-[2-[bis(carboxymethyl)amino]ethyl]-N-[2-oxo-2-[[2-[(2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl)oxy]ethyl]amino]ethyl]-, (S)- (9CI) (CA INDEX NAME)

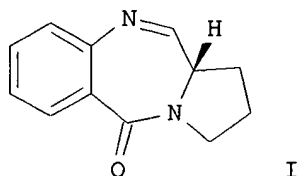
Absolute stereochemistry.

09/763,767



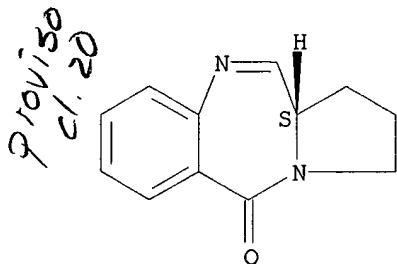
09/763,767

~~LA~~ 6 ANSWER 36 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1996:154392 CAPLUS  
DN 124:289058  
TI A new route for the synthesis of pyrrolo[2,1-c][1,4]benzodiazepine  
antibiotics via oxidation of cyclic secondary amine  
AU Kamal, Ahmed; Rao, N. Venugopal  
CS Indian Inst. Chem. Technol., Hyderabad, 500 007, India  
SO Chem. Commun. (Cambridge) (1996), (3), 385-6  
CODEN: CHCOFS; ISSN: 1359-7345  
DT Journal  
LA English  
OS CASREACT 124:289058  
GI



AB The synthesis of the imine-contg. pyrrolo[2,1-c][1,4]benzodiazepine  
DNA-binding antitumor antibiotics, e.g. I, was achieved by a new method of  
oxidn. of cyclic secondary amines which does not endanger the stereochem.  
integrity of the C-11a position.  
IT **72435-89-3P 81307-24-6P 175521-32-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of pyrrolo[2,1-c][1,4]benzodiazepine antibiotics via oxidn.  
of cyclic secondary amines)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

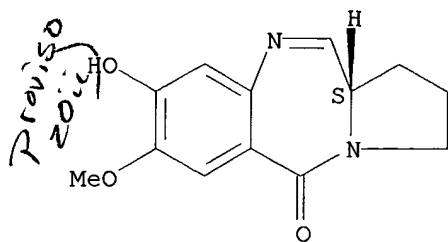
Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-  
7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

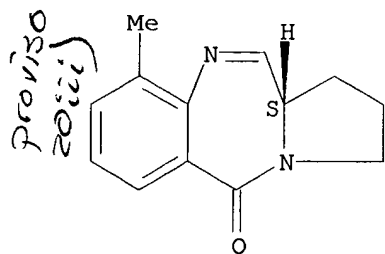
09/763,767



RN 175521-32-1 CAPLUS

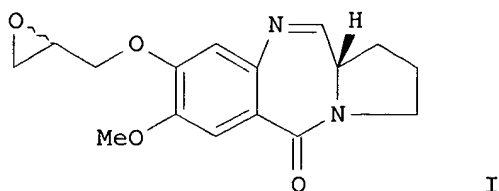
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methyl-,  
(11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



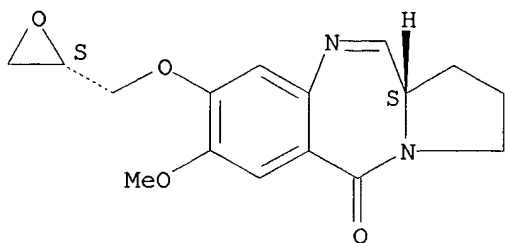
09/763,767

~~126~~ ANSWER 37 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1995:786320 CAPLUS  
DN 124:8772  
TI Design and synthesis of a novel epoxide-containing pyrrolo[2,1-  
c][1,4]benzodiazepine (PBD) via a new cyclization procedure  
AU Wilson, Stuart C.; Howard, Philip W.; Thurston, David E.  
CS Div. Med. Chem., Univ. Portsmouth, Portsmouth, Hants., PO1 2DZ, UK  
SO Tetrahedron Lett. (1995), 36(35), 6333-6  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 124:8772  
GI



AB The synthesis of a potential DNA-crosslinking pyrrolo[2,1-  
c][1,4]benzodiazepine I substituted at the C8-position with a  
2,3-epoxypropaneoxy moiety using a new cyclization procedure is described.  
IT **171002-52-1P 171229-23-5P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(design and synthesis of a novel epoxide-contg. pyrrolobenzodiazepine  
via a new cyclization procedure)  
RN 171002-52-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-  
8-[(2S)-oxiranylmethoxy]-, (11aS)- (9CI) (CA INDEX NAME)

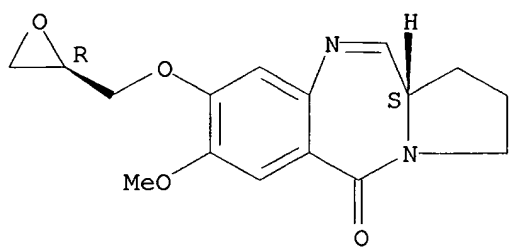
Absolute stereochemistry.



RN 171229-23-5 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-  
8-(oxiranylmethoxy)-, [R-(R\*,S\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

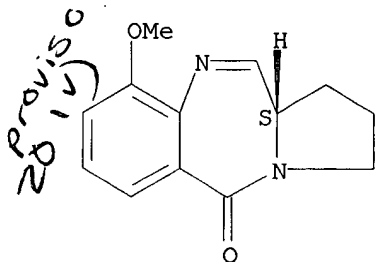
09/763,767



09/763,767

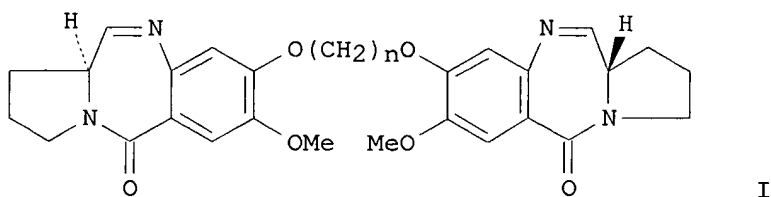
~~126~~ ANSWER 38 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1995:730623 CAPLUS  
DN 123:227886  
TI A stereoselective synthesis of tilivalline and its analogs utilizing a new Mannich type intramolecular cyclization  
AU Aoyama, Toyohiko; Shioiri, Takayuki  
CS Fac. Pharm. Sci., Nagoya City Univ., Nagoya, 467, Japan  
SO Yakugaku Zasshi (1995), 115(6), 446-59  
CODEN: YKKZAJ; ISSN: 0031-6903  
DT Journal  
LA Japanese  
OS CASREACT 123:227886  
AB Tilivalline (I), a metabolite isolated from *Klebsiella pneumoniae* var. oxytoca, belongs to a group of pyrrolo[2,1-c][1,4]benzodiazepines, a characteristic skeleton of anthramycin-type antitumor antibiotics. The authors have accomplished a completely stereoselective, efficient and convenient synthesis of I utilizing a new Mannich type intramol. cyclization as a key step. Further, a computational chem. anal. clarified the effect of zinc chloride on the high stereoselectivity in the tilivalline synthesis. To aim both the extension of the scope of the new Mannich type intramol. cyclization and the studies on the structure-biol. activity relationship, the authors further extended the method to the synthesis of tilivalline derivs. and 2-(3'-indolyl)-1,4-benzodiazepines. Investigation on the cytotoxicity of I and its analogs has revealed that I shows the strong cytotoxicity toward mouse leukemia L 1210 cells and the replacement of the indole function of I with cyano one increases the cytotoxicity of I about 100 times (IC<sub>50</sub> = 0.05 .mu.g/mL).  
IT **110715-89-4P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(stereoselective synthesis of tilivalline and analogs utilizing a new Mannich type intramol. cyclization)  
RN 110715-89-4 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

~~136~~ ANSWER 39 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1995:637534 CAPLUS  
DN 123:285962  
TI Facile and efficient synthesis of the dimers of DC-81 antitumor antibiotics  
AU Kamal, Ahmed; Rao, N. Venugopal  
CS Div. Org. Chem., Indian Inst. Chem. Technol., Hyderabad, 500 007, India  
SO Tetrahedron Lett. (1995), 36(24), 4299-302  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 123:285962  
GI



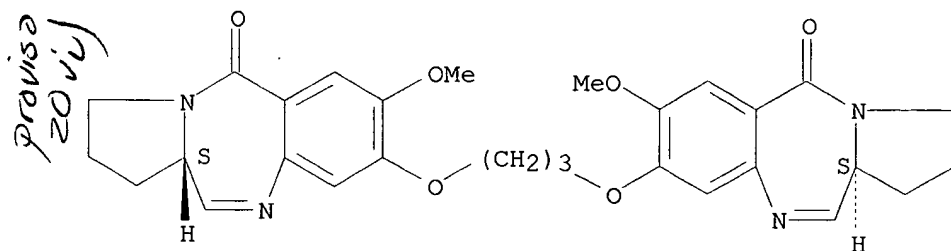
AB We report an improved, economical and versatile route to the dimers (I, n = 3, 4, 5) of DC-81 antitumor antibiotics. Particularly, the protection and deprotection steps in its synthesis and the prepn. of its precursors have been avoided. There is a significant improvement in the overall yields.

IT **169436-02-6P 169436-03-7P 169436-04-8P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of the dimers of DC-81 antitumor antibiotics)

RN 169436-02-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (R\*,R\*)- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



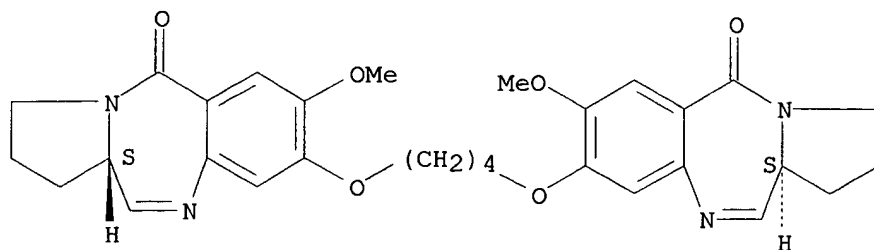
RN 169436-03-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,4-butanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (R\*,R\*)- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



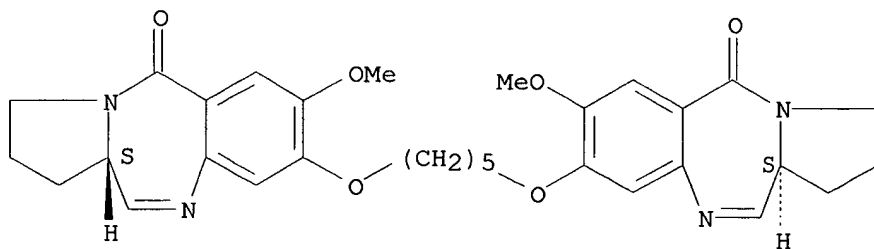
09/763,767



RN 169436-04-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanediylobis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (R\*,R\*)- (9CI)  
(CA INDEX NAME)

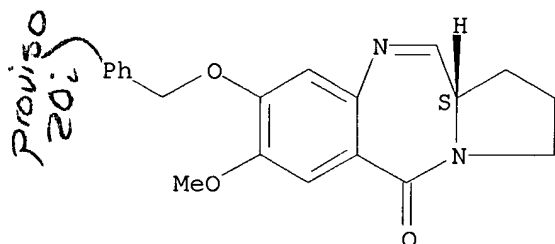
Relative stereochemistry.



09/763,767

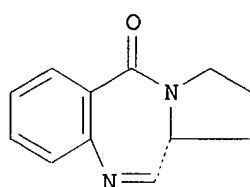
~~126~~ ANSWER 40 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1995:629801 CAPLUS  
DN 123:112029  
TI Facile Synthesis of 1,4-Benzodiazepin-5-one Derivatives via Intramolecular  
Aza-Wittig Reaction. Application to an Efficient Synthesis of O-Benzyl  
DC-81  
AU Eguchi, Shoji; Yamashita, Keizo; Matsushita, Yuji; Kakehi, Akikazu  
CS Faculty of Engineering, Nagoya University, Nagoya, 464-01, Japan  
SO J. Org. Chem. (1995), 60(13), 4006-12  
CODEN: JOCEAH; ISSN: 0022-3263  
DT Journal  
LA English  
AB The tandem Staudinger/aza-Wittig reaction of N-(o-azidobenzoyl)-.alpha.-  
amino acid esters gave the corresponding 1,4-benzodiazepin-5-one derivs.  
in moderate to good yields. This method was applied successfully to a new  
efficient synthesis of BzlDC-81.  
IT **127810-79-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(facile synthesis of benzodiazepinone derivs. via tandem  
Staudinger/aza-Wittig reaction)  
RN 127810-79-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-  
8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

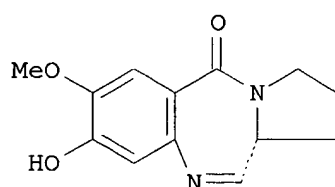


09/763,767

~~126~~ ANSWER 41 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1995:567326 CAPLUS  
DN 123:143505  
TI Synthesis of pyrrolo[2,1-c][1,4]benzodiazepines via an intramolecular  
aza-Wittig reaction. Synthesis of the antibiotic DC-81  
AU Molina, Pedro; Diaz, Isidora; Tarraga, Alberto  
CS Facultad Quimicas, Universidad Murcia, Murcia, E-30071, Spain  
SO Tetrahedron (1995), 51(19), 5617-30  
CODEN: TETRAB; ISSN: 0040-4020  
DT Journal  
LA English  
GI



I



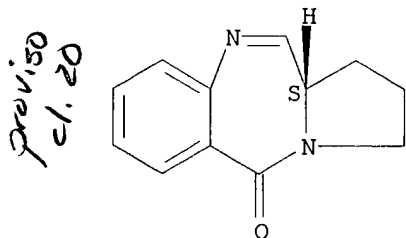
II

AB A new and efficient synthesis of the pyrrolo[2,1-c][1,4]benzodiazepine (PBD) ring system has been carried out using, as a key step, an intramol. aza Wittig reaction of the appropriately substituted N-(2-azidobenzoyl)pyrrolidine-2-carboxaldehydes. The parent unsubstituted PBD I and the natural product DC-81 II have been prepd. in the imine form in good overall yields.

IT **72435-89-3P 81307-24-6P, DC 81 127810-79-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(synthesis of pyrrolobenzodiazepines and DC-81 via intramol. aza-Wittig)

RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

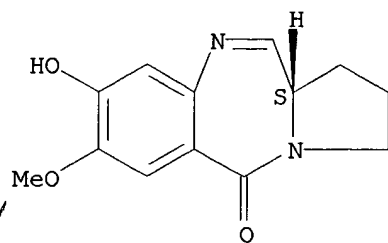
Absolute stereochemistry. Rotation (+).



RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

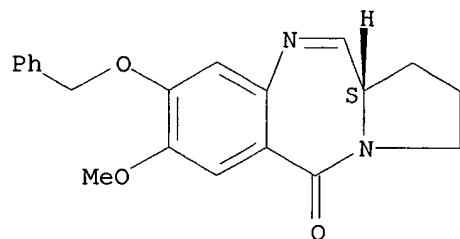
09/763,767



RN 127810-79-1 CAPLUS

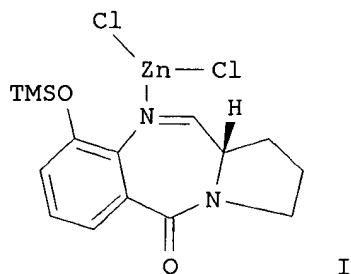
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



09/763,767

~~L26~~ ANSWER 42 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1995:213595 CAPLUS  
DN 122:56290  
TI Effect of zinc halides on the high stereoselectivity of a new Mannich type cyclization in the tilivalline synthesis. A computational chemical analysis  
AU Matsumoto, Takatoshi; Aoyama, Toyohiko; Shioiri, Takayuki; Osawa, Eiji  
CS Dep. Synthetic Org. Chem., Nagoya City Univ., Nagoya, 467, Japan  
SO Tetrahedron (1994), 50(32), 9775-80  
CODEN: TETRAB; ISSN: 0040-4020  
DT Journal  
LA English  
GI



AB The calcn. by the semi-empirical MO method concerning the effect of zinc halides on the high stereoselectivity of a new Mannich type cyclization in our tilivalline synthesis has revealed that (1) zinc chloride coordinates with the N10 atom during the reaction and (2) the steric hindrance on the .alpha. side and the extension of LUMO to the .beta. side in the intermediate I govern the high stereoselectivity.

IT 71444-83-2 110715-89-4 160094-61-1  
160094-62-2 160094-63-3 160094-64-4  
160094-65-5 160094-66-6 160094-67-7  
160117-37-3 160117-38-4 160117-39-5  
160117-40-8 160117-41-9 160117-42-0  
160117-43-1 160117-44-2 160117-45-3  
160117-46-4 160117-47-5 160117-48-6  
160117-49-7

RL: PRP (Properties)

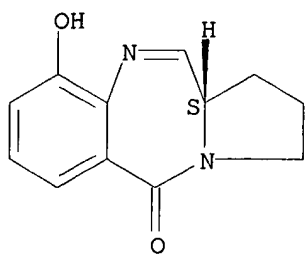
(MO calcs. on the effect of zinc halides on the stereoselectivity of a Mannich type cyclization in the tilivalline synthesis)

RN 71444-83-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

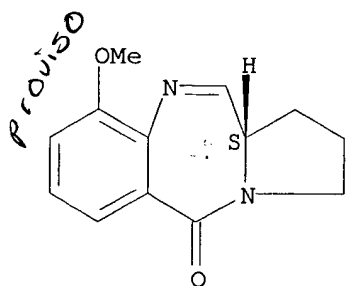
09/763,767



RN 110715-89-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

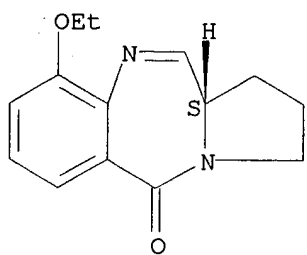
Absolute stereochemistry.



RN 160094-61-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-ethoxy-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

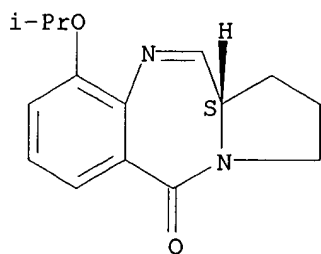


RN 160094-62-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-(1-methylethoxy)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

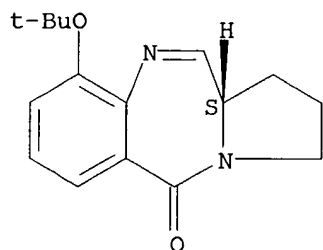
09/763,767



RN 160094-63-3 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-(1,1-dimethylethoxy)-  
1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

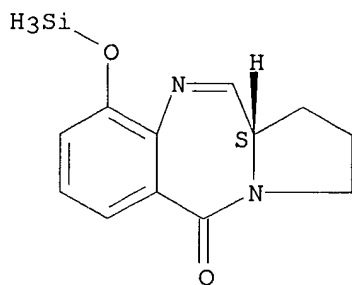
Absolute stereochemistry.



RN 160094-64-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-  
(silyloxy)-, (S)- (9CI) (CA INDEX NAME)

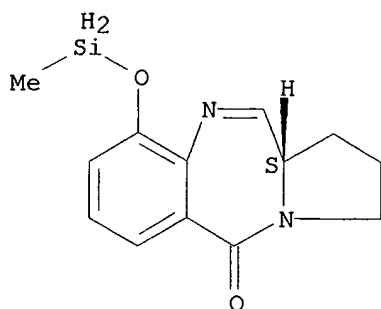
Absolute stereochemistry.



RN 160094-65-5 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-  
[(methylsilyl)oxy]-, (S)- (9CI) (CA INDEX NAME)

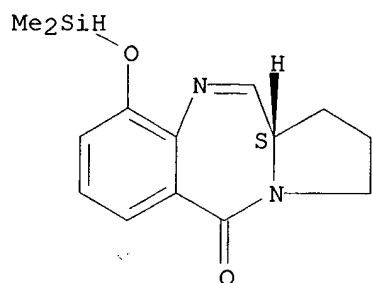
Absolute stereochemistry.



RN 160094-66-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-[(dimethylsilyl)oxy]-  
1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

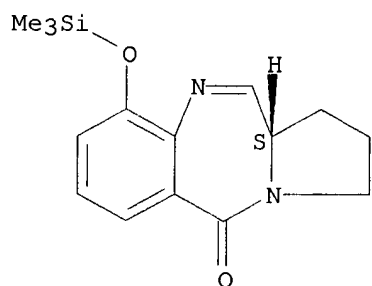
Absolute stereochemistry.



RN 160094-67-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-  
[(trimethylsilyl)oxy]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

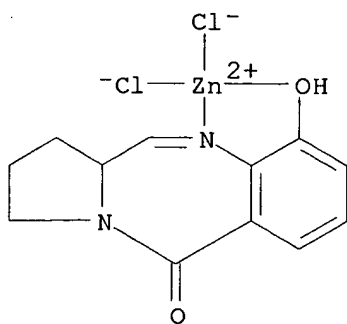


RN 160117-37-3 CAPLUS

CN Zinc, dichloro(1,2,3,11a-tetrahydro-9-hydroxy-5H-pyrrolo[2,1-  
c][1,4]benzodiazepin-5-one-N10,O9)-, [T-4-(S)]- (9CI) (CA INDEX NAME)

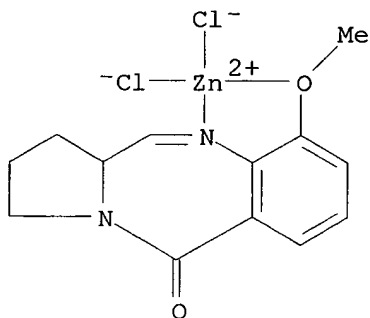


09/763,767



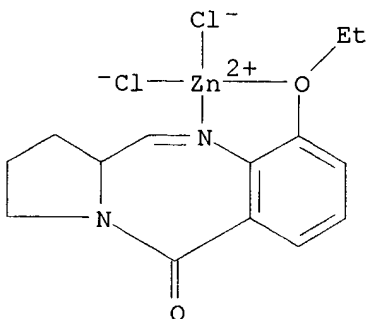
RN 160117-38-4 CAPLUS

CN Zinc, dichloro(1,2,3,11a-tetrahydro-9-methoxy-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9)-, [T-4-(S)]- (9CI) (CA INDEX NAME)



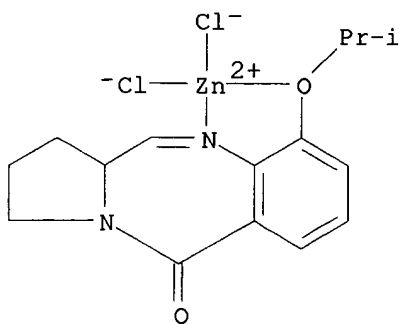
RN 160117-39-5 CAPLUS

CN Zinc, dichloro(9-ethoxy-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9)-, [T-4-(S)]- (9CI) (CA INDEX NAME)



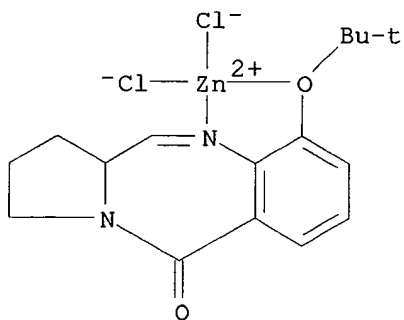
RN 160117-40-8 CAPLUS

CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-(1-methylethoxy)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



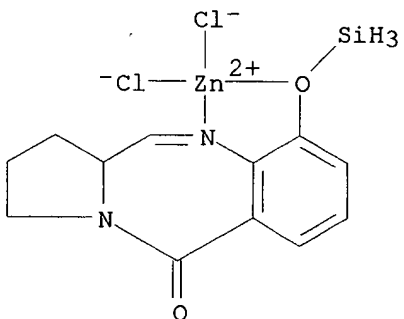
RN 160117-41-9 CAPLUS

CN Zinc, dichloro[9-(1,1-dimethylethoxy)-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,09]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



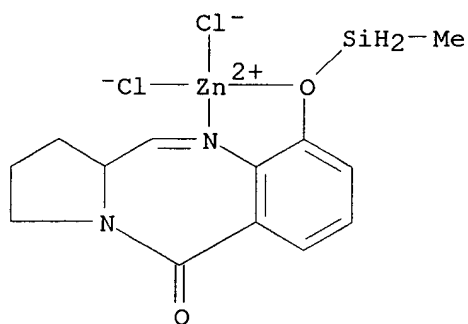
RN 160117-42-0 CAPLUS

CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-(silyloxy)-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,09]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



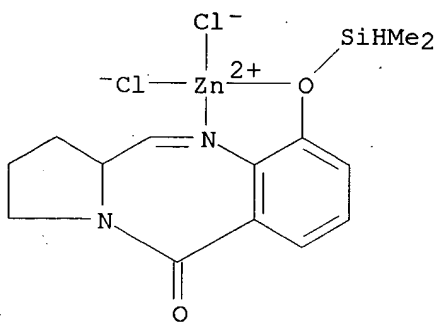
RN 160117-43-1 CAPLUS

CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-[(methylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,09]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



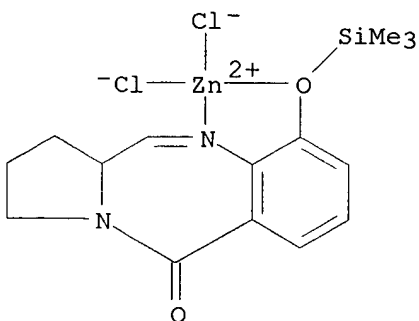
RN 160117-44-2 CAPLUS

CN Zinc, dichloro[9-[(dimethylsilyl)oxy]-1,2,3,11a-tetrahydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



RN 160117-45-3 CAPLUS

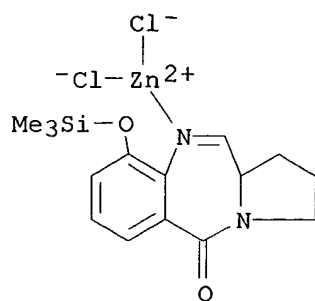
CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10,O9]-, [T-4-(S)]- (9CI) (CA INDEX NAME)



RN 160117-46-4 CAPLUS

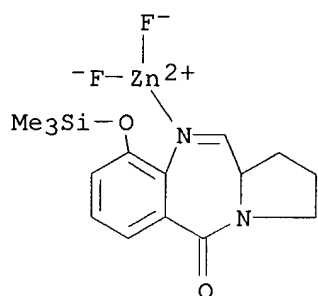
CN Zinc, dichloro[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10]-, (S)- (9CI) (CA INDEX NAME)

09/763,767



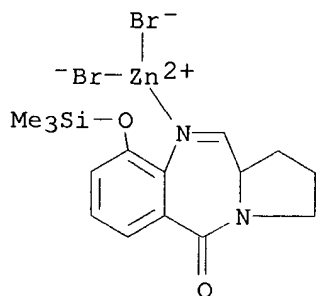
RN 160117-47-5 CAPLUS

CN Zinc, difluoro[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10]-, (S)- (9CI) (CA INDEX NAME)



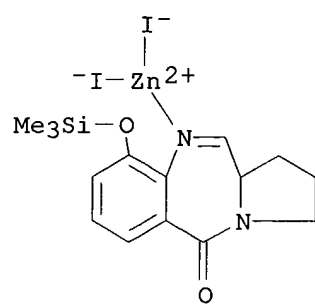
RN 160117-48-6 CAPLUS

CN Zinc, dibromo[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10]-, (S)- (9CI) (CA INDEX NAME)



RN 160117-49-7 CAPLUS

CN Zinc, diiodo[1,2,3,11a-tetrahydro-9-[(trimethylsilyl)oxy]-5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-one-N10]-, (S)- (9CI) (CA INDEX NAME)



09/763,767

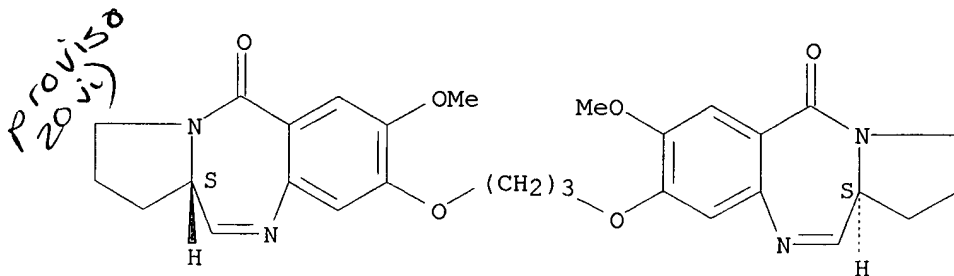
~~126~~ ANSWER 43 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1995:107251 CAPLUS  
~~DN~~ 122:97894  
TI DNA damage by anticancer agents and its repair: mapping in cells at the  
subgene level with quantitative polymerase chain reaction  
AU Grimaldi, Keith A.; Bingham, John P.; Souhami, Robert L.; Hartley, John A.  
CS Dep. Oncology, Univ. Coll. Long Med. Sch., London, W1P 8BT, UK  
SO Anal. Biochem. (1994), 222(1), 236-42  
CODEN: ANBCA2; ISSN: 0003-2697  
DT Journal  
LA English  
AB The quant. polymerase chain reaction (QPCR)-based assay was used to  
measure DNA damage and repair to a small (523 bp) fragment of the  
single-copy human N-ras gene in K562 cells. Compared with previous  
methods DNA prepn. from treated cells and the subsequent detection of the  
radioactive product were considerably simplified. The results  
demonstrated that QPCR can be used to measure damage in a small gene  
segment, caused by cisplatin, nitrogen, and quinacrine mustards. Drug-DNA  
adducts produced by two novel minor groove binding, sequence-specific  
mols. (AT-486 and DSB-120) could be detected at physiol. relevant concns.  
of drug. For both cis-platin and nitrogen mustard the concn. required to  
cause damage in cells were higher than those needed to cause equiv. damage  
in isolated DNA. In contrast both AT-488 and quinacrine mustard caused  
more damage at equimolar concns. in cells than in isolated DNA. DSB-120,  
which is closely related to AT-486, was found to be 15-fold less effective  
than the latter at causing damage in treated cells despite similar  
reactivity with isolated DNA. Repair of damage caused by quinacrine  
mustard to the same small gene fragment was found to proceed at a const.  
rate over 24 h. The QPCR assay presented here is a simple quant. method  
to measure damage and repair in subgene functional units such as  
promoters, introns, and exons.  
IT 160675-00-3, DSB 120  
RL: BAC (Biological activity or effector, except adverse); BIOL  
(Biological study)  
(drug-DNA adducts produced by two novel minor groove binding,  
sequence-specific mols. (AT-486 and DSB-120) could be detected at  
physiol. relevant concns. of drug by quant. PCR)  
RN 160675-00-3 CAPLUS

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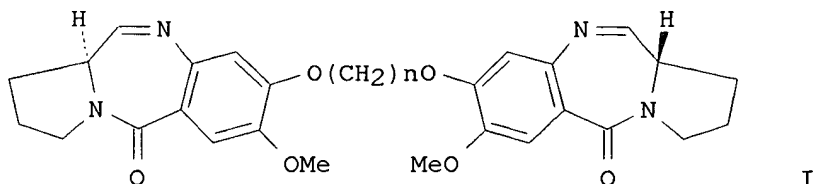
09/763,767

LA6 ANSWER 44 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1995:50719 CAPLUS  
DN 122:99738  
TI Development of anthramycin-based sequence-selective DNA crosslinking agents  
AU Jenkins, Terence C.; Neidle, Stephen; Thurston, David E.  
CS Cancer Res. Campaign Biomolecular Structure Unit, Inst. Cancer Res., Sutton/Surrey, SM2 5NG, UK  
SO Chem. Heterocycl. Compd., Proc. Symp., 11th (1993), 173-9. Editor(s): Stibor, Ivan. Publisher: Prague Inst. Chem. Technol., Prague, Czech. CODEN: 60BQAT  
DT Conference  
LA English  
AB Mol. modeling techniques, using double-stranded DNA as a template, have been used to design a series of potent and novel DNA crosslinking agents with useful G/C recognition properties. DNA reactivity has been confirmed using biophys. and biochem. assays, and qual. structure-activity correlations for cytotoxic potency have been demonstrated. NMR soln. studies provide a rational basis for the reactivity and DNA-crosslinking efficiency of the most reactive pyrrolobenzodiazepine dimer homolog, DSB-120. The predicted d(GATC) sequence preference for this agent, where the sequence contains a spanned ApT base tract, is substantiated by facile adduct formation with d(CICGATCICG).  
IT **140676-21-7**  
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study)  
(pyrrolobenzodiazepine dimer homolog; development of anthramycin-based sequence-selective DNA crosslinking agents)  
RN 140676-21-7 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



LA6 ANSWER 45 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1994:671426 CAPLUS  
 DN 121:271426  
 TI Cellular pharmacology of novel C8-linked anthramycin-based  
 sequence-selective DNA minor groove cross-linking agents  
 AU Smellie, M.; Kelland, L.R.; Thurston, D.E.; Souhami, R.L.; Hartley, J.A.  
 CS School, UCL Medical, London, W1P 8BT, UK  
 SO Br. J. Cancer (1994), 70(1), 48-53  
 CODEN: BJCAAI; ISSN: 0007-0920  
 DT Journal  
 LA English  
 GI



AB The cellular pharmacol. of a series of C8-linked pyrrolobenzodiazepine dimers with polymethylene linkers I ( $n = 3-6$ ) has been studied in a range of human tumor cell lines. The four compds. showed the same pattern of relative activity in five ovarian carcinoma cell lines and one cervical carcinoma cell line, which correlated with the previously demonstrated DNA interstrand crosslinking ability of the compds. in plasmid DNA. In human leukemic K562 cells the agents produced a block in the G2/M phase of the cell cycle characteristic of crosslinking drugs, and extensive interstrand crosslinking was obsd. in cells by alk. elution with no evidence of single-strand breaks. Cross-links continued to increase up to 24 h following a 1 h exposure to drug, and no repair was evident by 48 h. In a series of ovarian and cervical carcinoma cell lines with acquired resistance to cisplatin no cross-resistance to the most potent compd. I ( $n = 3$ ) was obsd. in two lines whose major mechanism of resistance to cisplatin was reduced platinum transport. Cross-resistance to 1 was obsd. in a cell line (A2780cisR) possessing elevated glutathione, and depletion of intracellular glutathione using D,L-buthionine-S,R-sulfoximine (BSO) from 10.25 nmol to 2.8 nmol  $10^{-6}$  cells reduced the level of resistance from 11-fold to 2-fold compared with sensitive cells. Crosslinking in the resistant cells was restored to 80% of the level in the parent line by BSO pretreatment. There was also a correlation between glutathione levels and sensitivity to 1 measured in several other ovarian cell lines. I ( $n = 3$ ) also showed cross-resistance in the doxorubicin-resistance cell line 41MdoxR and partial cross-resistance in CHldoxR cells. Both these lines possess elevated levels of p170 glycoprotein. Following treatment with 6  $\mu$ M verapamil, the resistance in these lines decreased almost 2-fold and 8-fold resp.

IT 140676-21-7 145325-56-0 145325-57-1  
 145325-58-2

RL: BAC (Biological activity or effector, except adverse); THU  
 (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (cellular pharmacol. of novel C8-linked anthramycin-based  
 sequence-selective DNA minor groove crosslinking agents)

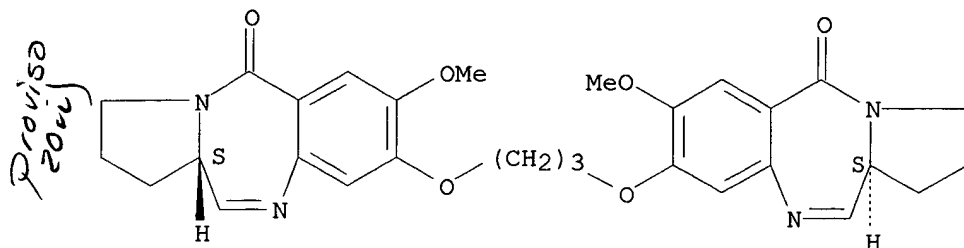
RN 140676-21-7 CAPLUS



09/763,767

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

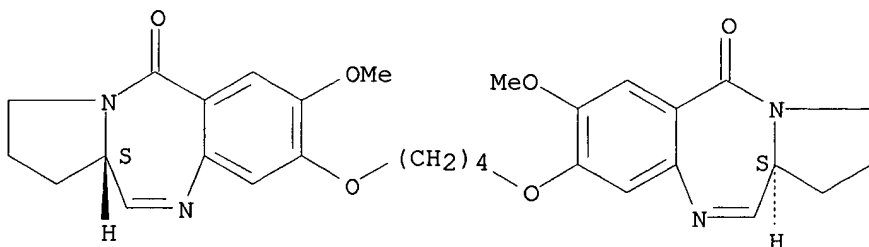
Absolute stereochemistry.



RN 145325-56-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,4-butanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

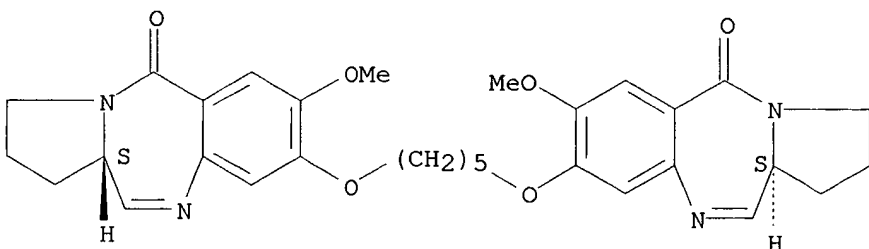
Absolute stereochemistry.



RN 145325-57-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanediybis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

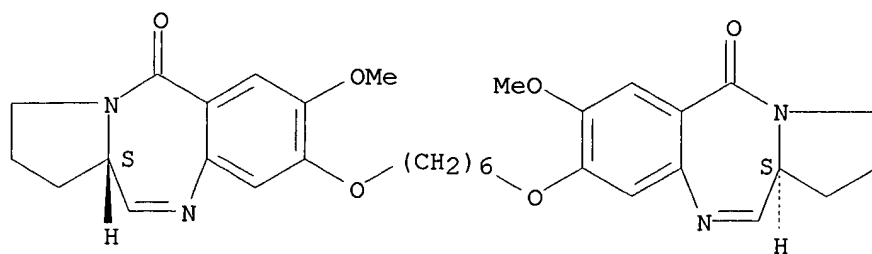


RN 145325-58-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,6-hexanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

09/763,767

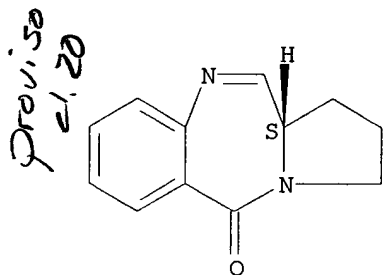
Absolute stereochemistry.



09/763,767

~~L20~~ ANSWER 46 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1994:528030 CAPLUS  
DN 121:128030  
TI Synthesis, DNA binding and crosslinking studies of  
pyrrolo[1,4]benzodiazepine dimers  
AU Zhang, Jundong  
CS Brown Univ., Providence, RI, USA  
SO (1993) 204 pp. Avail.: Univ. Microfilms Int., Order No. DA9407069  
From: Diss. Abstr. Int. B 1994, 54(10), 5159  
DT Dissertation  
LA English  
AB Unavailable  
IT **72435-89-3DP**, dimers  
RL: PREP (Preparation)  
(synthesis and DNA binding and crosslinking studies of)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



126 ANSWER 47 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1994:270468 CAPLUS

DN 120:270468

TI Anticancer pyrrolo[2,1-c][1,4]benzodiazepines

IN Thurston, David Edwin; Bose, Deverakonda Subhas

PA Cancer Research Campaign Technolgy Ltd., UK

SO PCT Int. Appl., 49 pp.

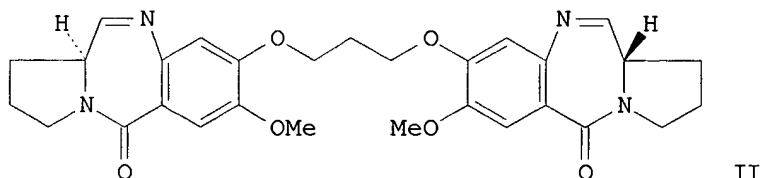
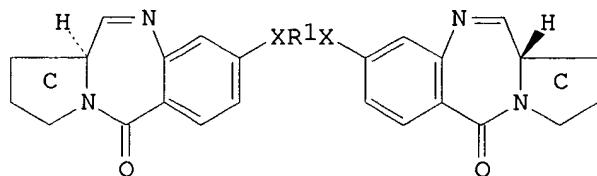
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9318045	A1	19930916	WO 1993-GB483	19930308
	W: AU, CA, JP, RU, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	ZA 9301637	A	19931004	ZA 1993-1637	19930308
	AU 9336435	A1	19931005	AU 1993-36435	19930308
PRAI	GB 1992-5051		19920309		
	WO 1993-GB483		19930308		
OS	MARPAT 120:270468				
GI					



AB The title compds. I [R1 = (un)substituted C3-12 alkylene; X = O, S, NH; the pyrrolobenzodiazepine ring may contain addnl. substituents in .gtoreq.1 of the 1, 2, 3, 6, 7, 9, and 11 positions and the C rings may optionally contain .gtoreq.1 addnl. hetero ring atom], which are capable of crosslinking double-stranded DNA and which are useful as anticancer agents, are prepd. Thus, pyrrolobenzodiazepine II, prepd. from vanillic acid in 7 steps, demonstrated 50% inhibitory concn. against L1210 mouse leukemia cells of 0.01 .mu.M and against ADJ/PC6 mouse plasma plasmacytoma of 0.0005 .mu.M.

IT **140676-21-7P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and anticancer activity of)

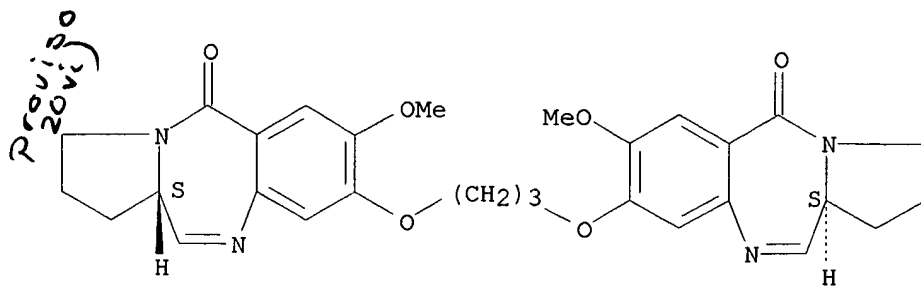
RN 140676-21-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-

09/763,767

(9CI) (CA INDEX NAME)

Absolute stereochemistry.

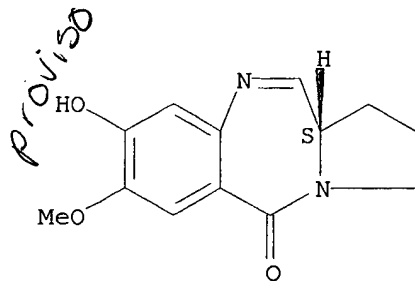


See 509107

09/763,767

126 ANSWER 48 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1994:235228 CAPLUS  
DN 120:235228  
TI A quantitative assay to measure the relative DNA-binding affinity of pyrrolo[2,1-c][1,4]benzodiazepine (PBD) antitumor antibiotics based on the inhibition of restriction endonuclease BamHI  
AU Puvvada, Madhu S.; Hartley, John A.; Jenkins, Terence C.; Thurston, David E.  
CS Sch. Pharm. Biomed. Sci., Univ. Portsmouth, Portsmouth, PO1 2DZ, UK  
SO Nucleic Acids Res. (1993), 21(16), 3671-5  
CODEN: NARHAD; ISSN: 0305-1048  
DT Journal  
LA English  
AB An assay has been developed (restriction endonuclease digestion assay-RED100) based on inhibition of the restriction endonuclease BamHI that is capable of quant. evaluation of the relative DNA-binding affinity of pyrrolo[2,1-c][1,4]benzodiazepine (PBD) antitumor antibiotics. This method provides comparable results to those obtained from thermal denaturation and ethidium bromide displacement assays but is much more sensitive, discriminating between mols. of similar structure such as DC-81, iso-DC-81 and neothramycin. The results reveal a trend between relative DNA-binding affinity and in vitro cytotoxicity for the PBDs in two tumor cell lines studied.  
IT **81307-24-6**, DC 81 **147778-99-2**, Iso-DC 81  
RL: PRP (Properties)  
(DNA binding affinity of, assay for, cytotoxicity in relation to)  
RN 81307-24-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

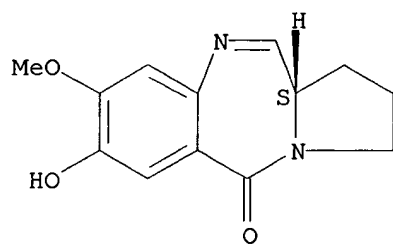
Absolute stereochemistry.



RN 147778-99-2 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-hydroxy-8-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

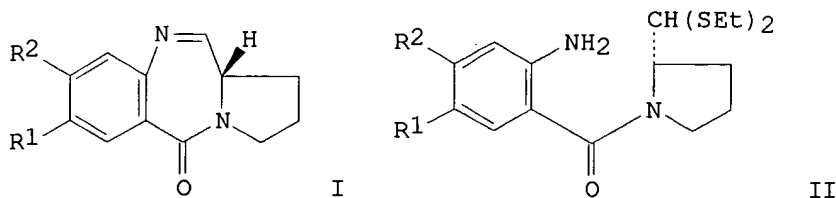
Absolute stereochemistry. Rotation (+).

09/763,767



09/763,767

~~L26~~ ANSWER 49 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1994:30583 CAPLUS  
DN 120:30583  
TI A new convenient procedure for the synthesis of pyrrolo[2,1-c][1,4]benzodiazepines  
AU Courtney, Stephen M.; Thurston, David E.  
CS Sch. Pharm. Biomed. Sci., Univ. Portsmouth, Portsmouth/Hants, PO1 2DZ, UK  
SO Tetrahedron Lett. (1993), 34(33), 5327-8  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 120:30583  
GI



AB An efficient synthesis of the pyrrolo[2,1-c][1,4]benzodiazepine (PDB) ring system based on a new cyclization procedure is reported. The parent unsubstituted PDB I (R1 = R2 = H) and the benzyl deriv. I (R1 = OMe, R2 = OCH2Ph) of the natural product DC-81 I (R1 = MeO, R2 = OH) have been synthesized to illustrate the utility of this procedure. Thus, amino dithioacetals II were prepd. and treated with SO2Cl2/SiO2/CH2Cl2 to give I (R1 = R2 = H; R1 = OMe, R2 = OCH2Ph).

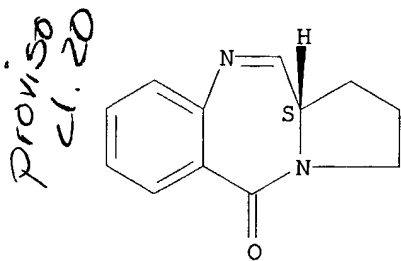
IT **72435-89-3P 151512-29-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 72435-89-3 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

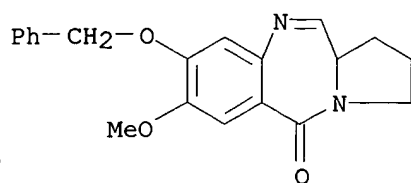
Absolute stereochemistry. Rotation (+).



RN 151512-29-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-  
8-(phenylmethoxy)- (9CI) (CA INDEX NAME)





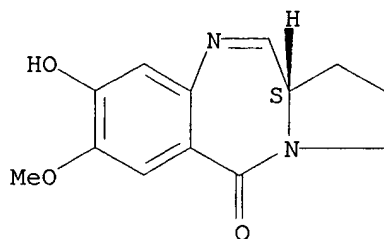
IT **81307-24-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of unsubstituted and benzyl derivs.)

RN 81307-24-6 CAPLUS

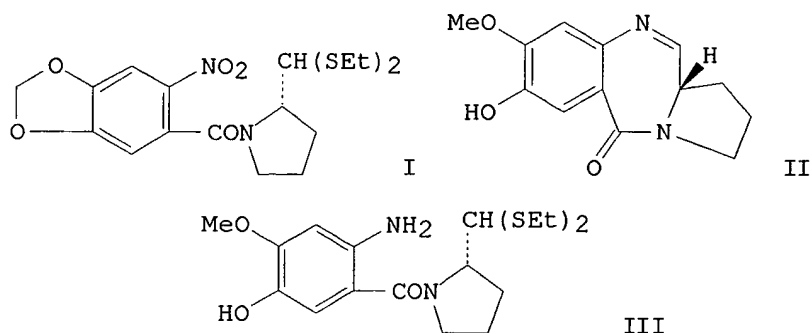
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

126 ANSWER 50 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1993:254878 CAPLUS  
DN 118:254878  
TI Tin dichloride-induced regiospecific opening of the 1,3-benzodioxole ring system: a route to the novel DNA-interactive ligand iso-DC-81  
AU Bose, D. Subhas; Thurston, David E.  
CS Sch. Pharm. Biomed. Sci., Univ. Portsmouth, Portsmouth, PO1 2DZ, UK  
SO Tetrahedron Lett. (1993), 34(8), 1377-8  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 118:254878  
GI



AB A novel tin-catalyzed regiospecific cleavage of a 1,3-benzodioxole ring system I is reported that has been applied to the synthesis of a uniquely substituted DNA-binding pyrrolo[2,1-c][1,4]benzodiazepine antitumor agent, iso-DC-81 (II). Thus, I was treated with  $\text{SnCl}_2$  in MeOH to give aminohydroxymethoxybenzamide III, which was cyclized with  $\text{HgCl}_2$  and  $\text{CaCO}_3$  in MeCN-H<sub>2</sub>O to give II.

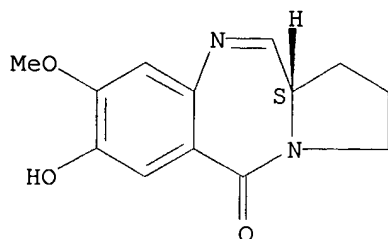
IT 147778-99-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., DNA-binding, and cytotoxicity of)

RN 147778-99-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-hydroxy-8-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

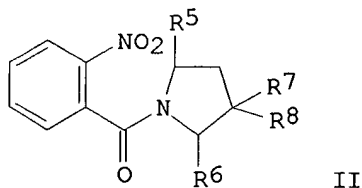
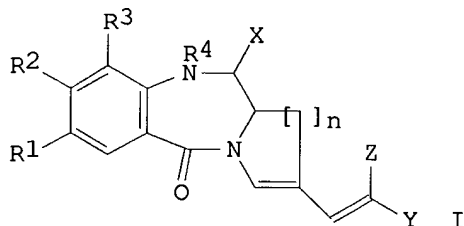
Absolute stereochemistry. Rotation (+).



09/763,767

~~26~~ ANSWER 51 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1993:147588 CAPLUS  
DN 118:147588  
TI Preparation of pyrrolo[1,4]benzodiazepines as antibiotics and antitumor agents  
IN Langlois, Nicole; Favre, Florence; Tempete-Gaillourdet, Christiane; Werner, Georges Hubert  
PA Centre National de la Recherche Scientifique, Fr.  
SO PCT Int. Appl., 24 pp.  
CODEN: PIXXD2  
DT Patent  
LA French  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9219620	A1	19921112	WO 1992-FR410	19920506
	W: CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
	FR 2676230	A1	19921113	FR 1991-5636	19910507
	FR 2676230	B1	19930827		
PRAI	FR 1991-5636		19910507		
OS	MARPAT 118:147588				
GI					



AB Title compds. (I; R1-R3 = H, halo, OH, alkoxy, etc.; R1 may addnl. = O-1'-sibrosamine; R4 = H, alkyl, alkanoyl; X = H, OH, alkoxy, NH2, etc.; R4X = bond; Y, Z = H, alkyl, alkoxy, alkoxy, CONH2, etc.; R4X = bond; Y, Z = H, alkyl, alkoxy, alkoxy, CONH2, etc.; n = 1 or 2) were prep'd. Thus, nitrobenzamide II (R5 = CH2OAc, R6 = OMe, R7 = R8 = H) was converted in 5 steps to I (R1-R3 = Z = H, Y = CONMe2, n = 1) (III; R4X = bond). III (R4 = H, X = OMe) had MIC of .apprx. 60 mg/mL against Staphylococcus.

IT **146374-66-5P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, as antibiotic and antitumor agent)

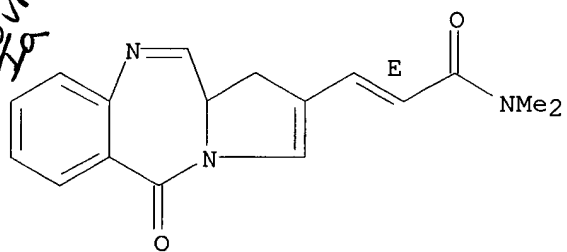
RN 146374-66-5 CAPLUS

CN 2-Propenamide, 3-(5,11a-dihydro-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)-N,N-dimethyl-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

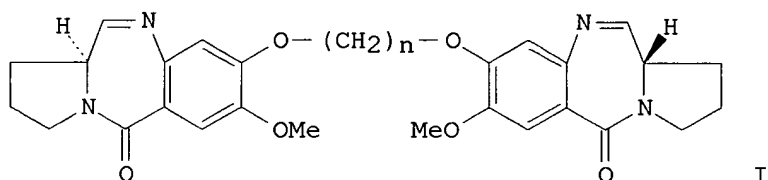
09/763,767

Proviso  
1a



09/763,767

~~IX~~ 6 ANSWER 52 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1993:59681 CAPLUS  
DN 118:59681  
TI Effect of linker length on DNA-binding affinity, cross-linking efficiency  
and cytotoxicity of C8-linked pyrrolobenzodiazepine dimers  
AU Bose, D. Subhas; Thompson, Andrew S.; Smellie, Melissa; Berardini, Mark  
D.; Hartley, John A.; Jenkins, Terence C.; Neidle, Stephen; Thurston,  
David E.  
CS Sch. Pharm. Biomed. Sci., Univ. Portsmouth, Portsmouth, PO1 2DZ, UK  
SO J. Chem. Soc., Chem. Commun. (1992), (20), 1518-20  
CODEN: JCCCAT; ISSN: 0022-4936  
DT Journal  
LA English  
OS CASREACT 118:59681  
GI



AB An efficient synthesis of a homologous series of C8-linked pyrrolobenzodiazepine dimers I ( $n = 3-6$ ) in 8 steps starting from vanillic acid is reported. I ( $n = 3, 5$ ), with an odd no. of methylenes in the linker show a higher affinity for DNA, enhanced crosslinking efficiency, and are more cytotoxic compared with I ( $n = 4, 6$ ).

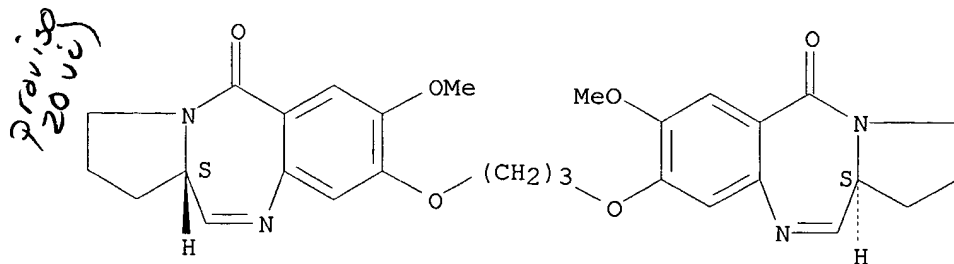
IT **140676-21-7P 145325-56-0P 145325-57-1P**  
**145325-58-2P**

RL: ADV (Adverse effect, including toxicity); SPN (Synthetic preparation);  
BIOL (Biological study); PREP (Preparation)  
(prepn. and binding with DNA and cytotoxicity of)

RN 140676-21-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

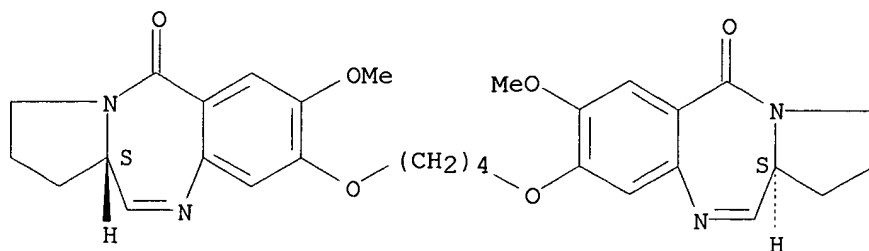


RN 145325-56-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,4-butanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

09/763,767

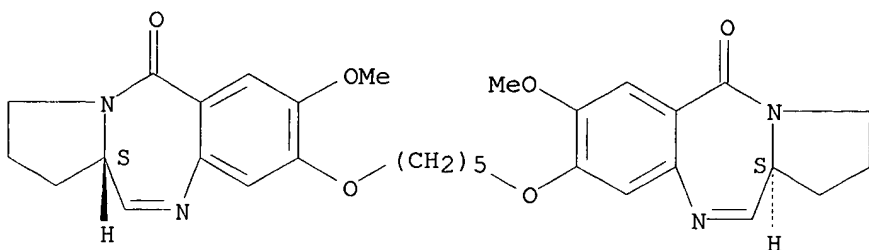
Absolute stereochemistry.



RN 145325-57-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,5-pentanedibis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

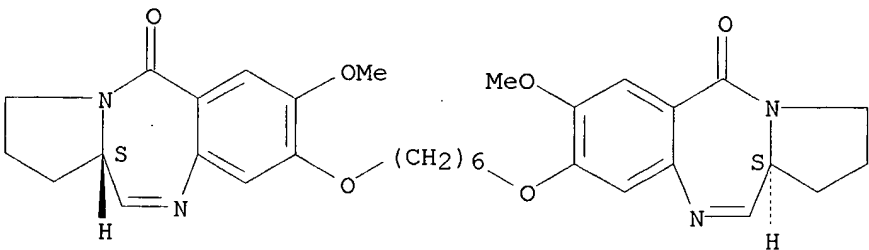
Absolute stereochemistry.



RN 145325-58-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,6-hexanedibis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

~~LS~~ 6 ANSWER 53 OF 107 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1992:483006 CAPLUS

~~DN~~ 117:83006

TI Template-directed design of a DNA-DNA crosslinker based upon a bis-tomaymycin-duplex adduct

AU Wang, Jeh Jeng; Hill, G. Craig; Hurley, Laurence H.

CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA

SO J. Med. Chem. (1992), 35(16), 2995-3002

CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

AB A template-directed approach to the design of a DNA-DNA interstrand cross-linker based upon the structure of a bis-tomaymycin-duplex adduct has been carried out. Tomaymycin is a member of the pyrrolo[1,4]benzodiazepines antitumor antibiotics. In a previous study it was shown that two tomaymycin mols. can be covalently bound to a 12-mer duplex mol., where the drug mols. are on opposite strands six base-pairs apart, and the stereochem. at the drug bonding site, and orientation in the minor groove, was defined by high-field NMR. This bis-tomaymycin 12-mer duplex adduct maintains the self-complementarity of the duplex and a B-type structure. In the present study it was shown using high-field NMR that this same 12-mer sequence can be truncated by two base pairs so that the two tomaymycin-modified guanines are now only four base-pairs apart, the two species of tomaymycin mols. are still bound with the same stereochem. and orientation, and the 10-mer duplex adduct maintains its self-complementarity. In a second 10-mer duplex it was shown that changing the bonding sequence from 5'CGA to 5'AGC does not significantly affect the structure of the bis-tomaymycin-duplex adduct. However, when the sequence is rearranged so that the drugs point in a tail-to-tail orientation rather than in the previous head-to-head configuration, there are more than one species of tomaymycin bound to DNA, and, as a consequence, the bis-tomaymycin 10-mer duplex adduct loses its self-complementarity. The 10-mer duplex contg. the 5'CGA sequence, in which the tomaymycin mols. are oriented head to head was used to design an interstrand crosslinking species in which the two drug mols. are linked together with a flexible linker mol.

IT 140676-21-7

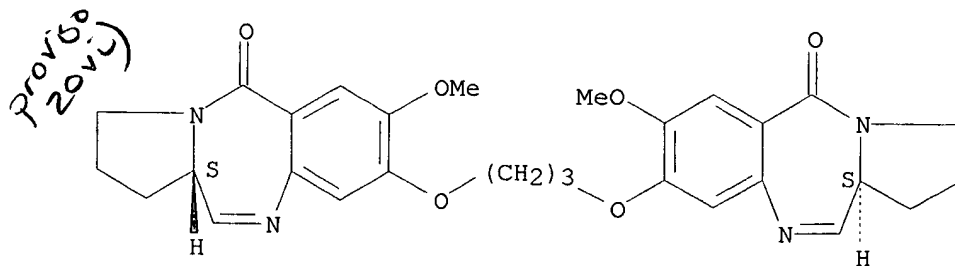
RL: BIOL (Biological study)

(as DNA-DNA interstand crosslinker, design of, tomaymycin-deoxyoligonucleotide adduct in relation to)

RN 140676-21-7 CAPLUS

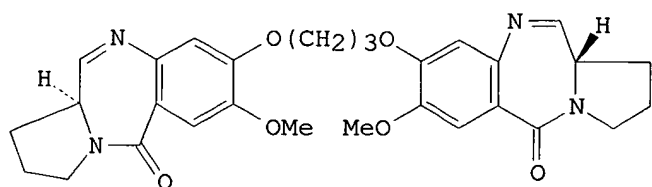
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/7/63,767

~~106~~ ANSWER 54 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1992:255585 CAPLUS  
DN 116:255585  
TI Rational design of a highly efficient irreversible DNA interstrand  
cross-linking agent based on the pyrrolobenzodiazepine ring system  
AU Bose, D. Subhas; Thompson, Andrew S.; Ching, Jingshan; Hartley, John A.;  
Berardini, Mark D.; Jenkins, Terence C.; Neidle, Stephen; Hurley, Laurence  
H.; Thurston, David E.  
CS Sch. Pharm. Biomed. Sci., Portsmouth Polytech., Portsmouth, PO1 2DZ, UK  
SO J. Am. Chem. Soc. (1992), 114(12), 4939-41  
CODEN: JACSAT; ISSN: 0002-7863  
DT Journal  
LA English  
GI



I

AB Pyrrolo[2,1-c][1,4]benzodiazepine C8 dimer DSB-120 (I) was prepd. and its DNA binding studied. I is a remarkably efficient crosslinking agent, showing activity down to at least 0.01 .mu.M and >90% crosslinking at 0.4 .mu.M. Extensive modeling studies of I with d(CGYGXXCYCG)2 show that the spatial sepn. of the pyrrolobenzodiazepine units is optimal for spanning 6 base pairs with a preference for 5'-PuGATCPy or 5'-PyGATCPu sequences, and that it actively recognizes the embedded d(GTAC)2 sequence. 1H NMR of the 1:1 adduct of I and the self-complementary 10-mer d(CICGATCICG)2 showed that the duplex is crosslinked sym. via the minor groove N2 positions of the guanines, with 11S,11S' stereochem. in the ligand, and minor distortion of the helix.

IT 81307-24-6, Antibiotic DC 81

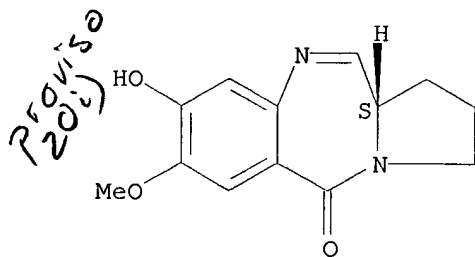
RL: RCT (Reactant)

(antitumor and DNA binding activities of)

RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 140676-21-7P



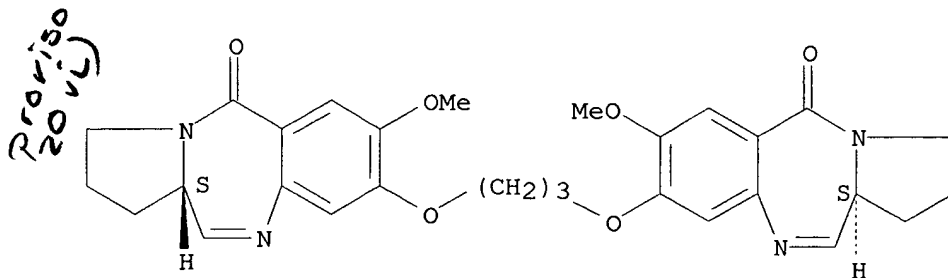
09/763,767

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., antitumor, and DNA binding activities of)

RN 140676-21-7 CAPLUS

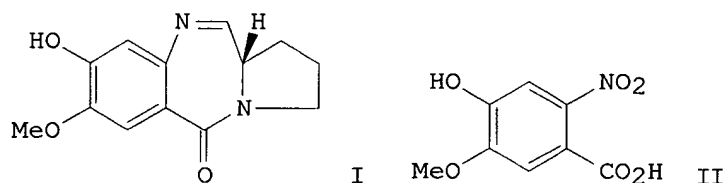
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8,8'-[1,3-propanediylbis(oxy)]bis[1,2,3,11a-tetrahydro-7-methoxy-, (11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

~~LN~~ 6 ANSWER 55 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1992:193997 CAPLUS  
DN 116:193997  
TI New approaches to pyrrolo[2,1-c][1,4]benzodiazepines: synthesis,  
DNA-binding and cytotoxicity of DC-81  
AU Rose, D. Subhas; Jones, Gary B.; Thurston, David E.  
CS Sch. Pharm. Biomed. Sci., Portsmouth Polytech., Portsmouth/Hants., PO1  
2DZ, UK  
SO Tetrahedron (1992), 48(4), 751-8  
CODEN: TETRAB; ISSN: 0040-4020  
DT Journal  
LA English  
OS CASREACT 116:193997  
GI



AB Two routes to the naturally occurring DNA-binding antitumor antibiotic DC-81 (I) are described, one of which involves a novel cyclization process based on acid resin. The second route involves the synthesis of a new compd., 6-nitrovanillic acid (II), a key A-ring component of many naturally occurring title compds. These routes have provided a sufficient quantity of DC-81 to allow complete characterization and evaluation in DNA-binding and in vitro cytotoxicity studies.

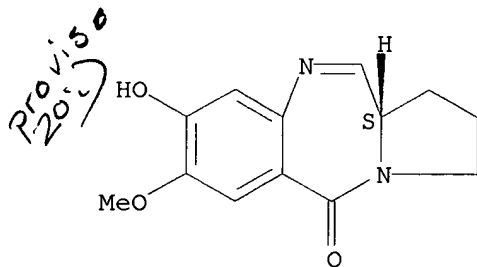
IT **81307-24-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn., DNA-binding and cytotoxicity of)

RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

~~L26~~ ANSWER 56 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1992:99301 CAPLUS

DN 116:99301

TI Maleic anhydride copolymers as antidotes for the cytotoxicity of neoplasm inhibitors

IN Bach, Ardalan; Shanahan, William R., Jr.

PA Searle, G. D., and Co., USA

SO Eur. Pat. Appl., 27 pp.

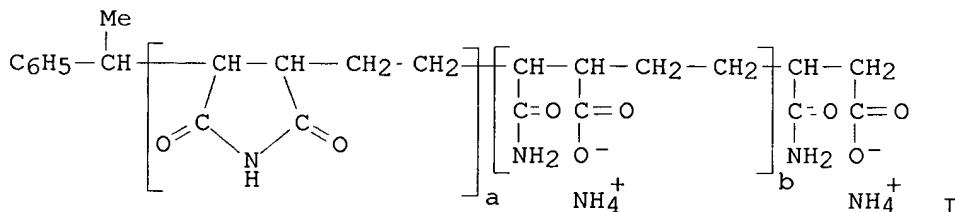
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 393575	A1	19901024	EP 1990-107246	19900417
	EP 393575	B1	19940316		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2014732	AA	19901017	CA 1990-2014732	19900417
	JP 02292227	A2	19901203	JP 1990-101530	19900417
	AT 102838	E	19940415	AT 1990-107246	19900417
	ES 2062155	T3	19941216	ES 1990-107246	19900417
PRAI	US 1989-339503		19890417		
	EP 1990-107246		19900417		
OS	MARPAT 116:99301				
GI					



AB Half-amide:half-imide copolymers comprising ethylene and maleic anhydride moieties (structure given), specifically carbetimer (I; a/b = 1:2-5), decrease the cytotoxic side effects of neoplasm inhibitors. Mice treated i.v. with 21 mg adriamycin/kg died within 5 days. When 1700 mg I/kg was administered concomitantly, no lethality was shown for >30 days.

IT **117782-84-0**, Sibanomicin

RL: PRP (Properties)

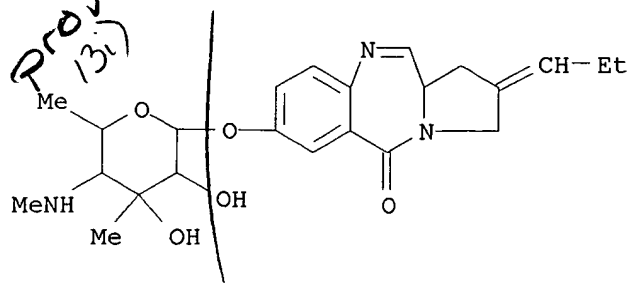
(cytotoxicity of, maleic anhydride copolymer antidote for)

RN 117782-84-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-propylidene-, (2E)- (9CI) (CA INDEX NAME)

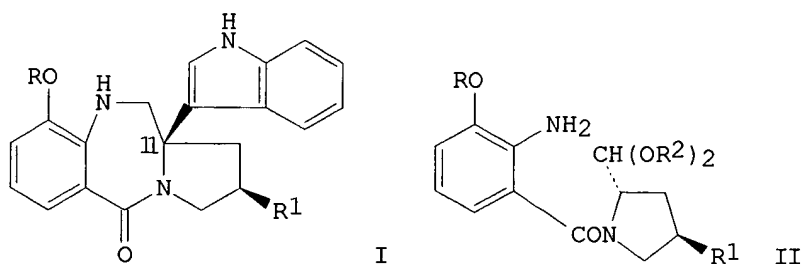
09/763,767

Proviso  
(31)



09/763,767

~~LE~~ 6 ANSWER 57 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1991:535788 CAPLUS  
DN 115:135788  
TI New methods and reagents in organic synthesis. 92. A stereoselective synthesis of tilivalline and its analogs  
AU Mori, Shigehiro; Ohno, Tomoyasu; Harada, Hiroshi; Aoyama, Toyohiko; Shioiri, Takayuki  
CS Fac. Pharm. Sci., Nagoya City Univ., Nagoya, 467, Japan  
SO Tetrahedron (1991), 47(27), 5051-70  
CODEN: TETRAB; ISSN: 0040-4020  
DT Journal  
LA English  
OS CASREACT 115:135788  
GI



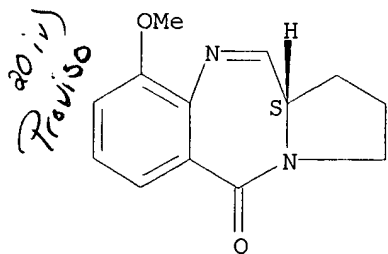
AB Tilivalline I (R = R1 = H) and its derivs. I (R = H, Me, PhCH2; R1 = H, HO, PhCH2O) were efficiently and stereoselectively prepd. The key step was the one-pot intramol. cyclocondensation of aminobenzoylpyrrolidinecarboxamides II (R2 = Me, Et) and stereoselective addn. of indole. The use of different nucleophiles gave a series of 11-substituted 5H-pyrrolo[2,1-c][1,4]benzodiazepin-5-ones.

IT **110715-89-4P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and addn. reaction of, with indole)

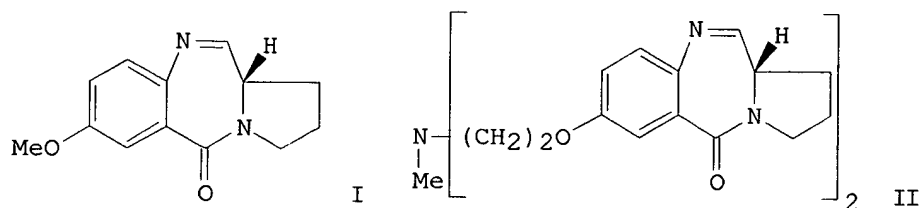
RN 110715-89-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L26 ANSWER 58 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1991:239940 CAPLUS  
 DN 114:239940  
 TI DNA binding properties of a new class of linked anthramycin analogs  
 AU Farmer, J. Dean, Jr.; Gustafson, Gary R.; Conti, Andrea; Zimm, Matthew B.;  
 Suggs, J. William  
 CS Dep. Chem., Brown Univ., Providence, RI, 02912, USA  
 SO Nucleic Acids Res. (1991), 19(4), 899-904  
 CODEN: NARHAD; ISSN: 0305-1048  
 DT Journal  
 LA English  
 GI



AB The DNA-binding properties of the anthramycin analogs I, II, and III were studied using fluorescence spectroscopy. A considerable fluorescence enhancement occurs when pyrrolo[1,4]benzodiazepines (P[1,4]Bs) are covalently attached to duplex DNA, which was used to show that neither the presence of RNA, single-stranded DNA, or protein had any effect on the degree of fluorescence enhancement resulting from the incubation of II and III with DNA. The enhancement was found to be dependent on the presence of the imine functionality in each of the compds. A wavelength of 320 nm was used to excite the chromophore and its emission wavelength max. was 420 nm. Addnl., it was discovered that the P[1,4]B ring system exhibits exceptionally favorable fluorescence polarization anisotropy (FPA) decay characteristics. For these more detailed fluorescence measurements, the structurally simpler analog I was used. The time-resolved max. FPA for I in glycerol at 25.degree. is 0.28. This result indicates that the P[1,4]B family of antibiotics could serve as sensitive probes of DNA dynamics in the 0.1 to 35 ns time scale.

IT **133954-34-4 133954-35-5 133954-36-6**

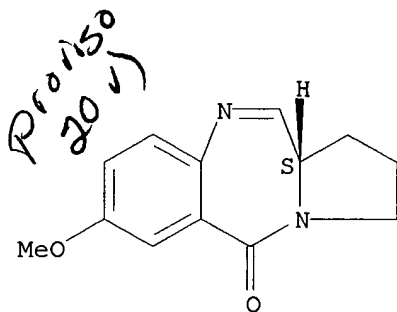
RL: BIOL (Biological study)  
 (binding of, to DNA, characterization of)

RN 133954-34-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

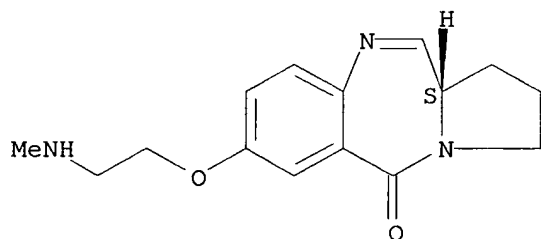
09/763,767



RN 133954-35-5 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-[2-(methoxymethylamino)ethoxy]-, (S)- (9CI) (CA INDEX NAME)

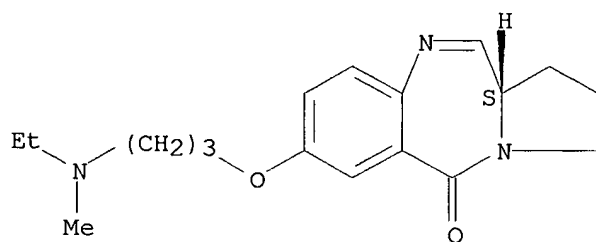
Absolute stereochemistry.



RN 133954-36-6 CAPLUS

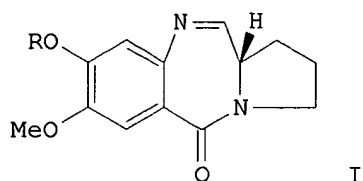
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[3-(ethylmethylamino)propoxy]-, 1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

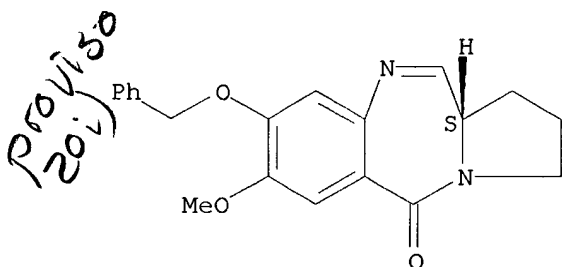
~~126~~ ANSWER 59 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1990:423460 CAPLUS  
DN 113:23460  
TI O-Debenzylation of a pyrrolo[2,1-c][1,4]benzodiazepine in the presence of  
a carbinolamine functionality: synthesis of DC-81  
AU Thurston, David E.; Murty, Varanasi S.; Langley, David R.; Jones, Gary B.  
CS Sch. Pharm., Portsmouth Polytech., Hants, PO1 2DZ, UK  
SO Synthesis (1990), (1), 81-4  
CODEN: SYNTBF; ISSN: 0039-7881  
DT Journal  
LA English  
OS CASREACT 113:23460  
GI



AB In contrast to other methods of redn., catalytic transfer hydrogenation allows debenzoylation of a phenolic hydroxyl in a carbinolamine-contg. pyrrolo[2,1-c][1,4]benzodiazepine, while leaving the biol.-important carbinolamine moiety intact. This has been demonstrated by synthesis of DC-81 (I, R = H) from 3,4-MeO(HO)C<sub>6</sub>H<sub>3</sub>CO<sub>2</sub>H via 4-benzyloxy-5-methoxy-2-nitrobenzoic acid and I (R = CH<sub>2</sub>Ph).

IT **127810-79-1P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and debenzoylation of, by mercuric chloride-calcium carbonate)  
RN 127810-79-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-8-(phenylmethoxy)-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

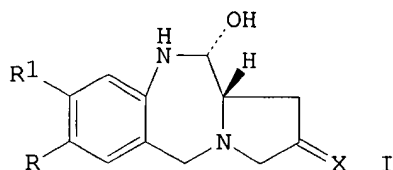


IT **89824-22-6P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 89824-22-6 CAPLUS



09/763,767

~~126~~ ANSWER 60 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1989:632415 CAPLUS  
DN 111:232415  
TI Photochemical approach to the synthesis of the pyrrolo[1,4]benzodiazepine antibiotics  
AU Weidner-Wells, Michele A.; DeCamp, Ann; Mazzocchi, Paul H.  
CS Dep. Chem. Biochem., Univ. Maryland, College Park, MD, 20742, USA  
SO J. Org. Chem. (1989), 54(24), 5746-58  
CODEN: JOCEAH; ISSN: 0022-3263  
DT Journal  
LA English  
OS CASREACT 111:232415  
GI



AB The total syntheses of the pyrrolo[1,4]benzodiazepine antitumor antibiotics prothracarcin I (X = CHMe, R = R1 = H), and DC-81 I (X = H2, R = OMe, R1 = OH) were realized using, as a key step, the photochem. [2.sigma. + 2.pi.] ring expansion of the appropriately substituted N-pentenylphthalimide to afford the corresponding pyrrolobenzazepinedione. Conversion of the photoproduct into the antibiotic skeleton was effected by transformation of the benzylic ketone into a carbinolamine via a Curtius rearrangement sequence.

IT **123355-35-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

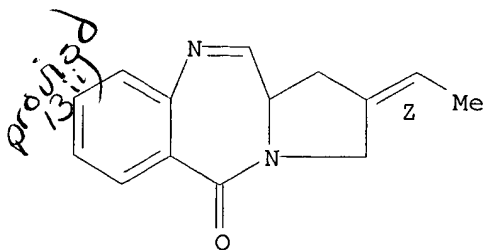
RN 123355-35-1 CAPLUS

IT **105498-28-0P 105498-29-1P 123355-42-0P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(total synthesis of)

RN 105498-28-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

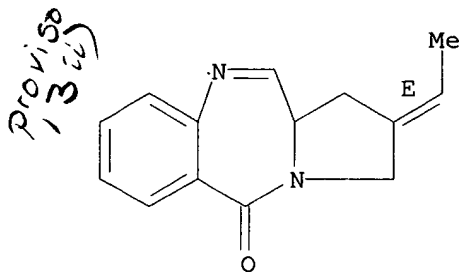


RN 105498-29-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (E)- (9CI) (CA INDEX NAME)

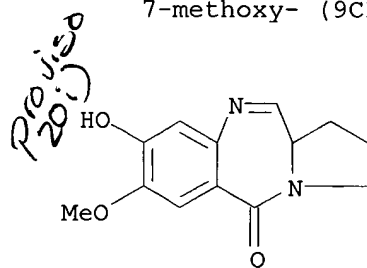
09/763,767

Double bond geometry as shown.



RN 123355-42-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy- (9CI) (CA INDEX NAME)



09/163,767

126 ANSWER 61 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1989:630672 CAPLUS

DN 111:230672

TI Novel anticancer antibiotic DC-105 and its manufacture with Streptomyces  
IN Nakano, Hirofumi; Takahashi, Isami; Asano, Kozo; Koda, Mayumi; Ashizawa, Tadashi

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp.

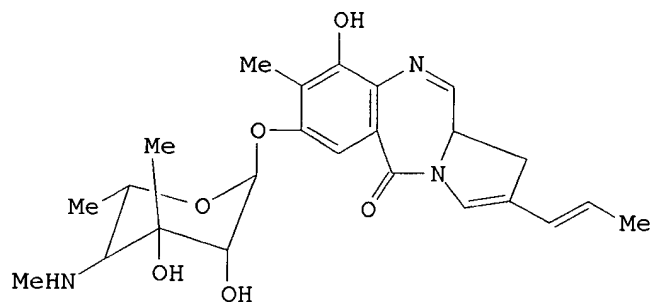
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 01121296	A2	19890512	JP 1987-277696	19871102
GI					



AB Anticancer antibiotic DC-105 (I) is manufd. by cultivation of I-producing Streptomyces. The culture medium was filtered, and the filtrate (100 L) was subjected to a series of chromatog. columns to produce 28 mg I, which at 0.03 mg/kg i.p. showed 128% T/C (treated group/control group) survival time in lymphocytic leukemia P-388-bearing mice, vs. 151%, for mitomycin C at 6 mg/kg. Streptomyces DO-105 was shake-cultured in a medium contg. tryptone, yeast ext., meat ext., hydrolyzable starch, glucose, and CaCO<sub>3</sub>; then aerobically shake-cultured in a medium contg. dextrin, soybean powder, and salts at 28.degree. for 70 h. An injection soln. was formulated contg. 10 mg I and .apprx.10 mL physiol. saline soln.

IT 123731-93-1P, Antibiotic DC 105

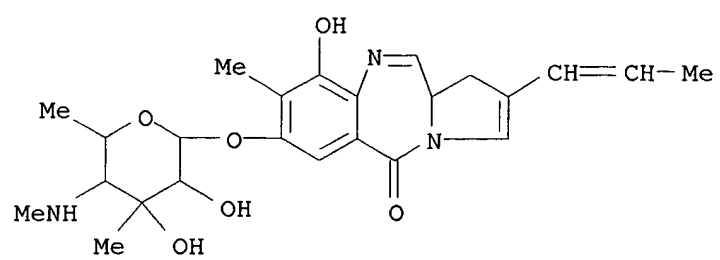
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)

(manuf. of, with Streptomyces DO-105, anticancer activity of)

RN 123731-93-1 CAPLUS

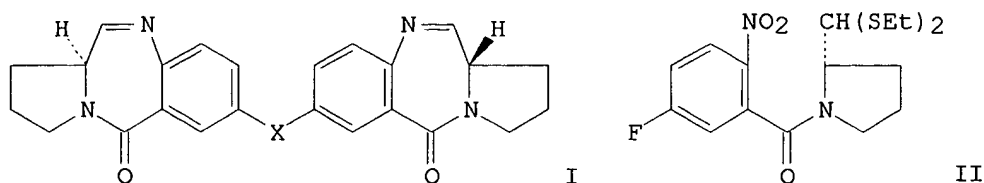
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,11a-dihydro-9-hydroxy-8-methyl-2-(1-propenyl)- (9CI) (CA INDEX NAME)

09/763,767



09/763,767

126 ANSWER 62 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1989:573848 CAPLUS  
DN 111:173848  
TI Synthesis and DNA crosslinking ability of a dimeric anthramycin analog  
AU Farmer, J. Dean, Jr.; Rudnicki, Suzanne M.; Suggs, J. William  
CS Dep. Chem., Brown Univ., Providence, RI, 02912, USA  
SO Tetrahedron Lett. (1988), 29(40), 5105-8  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 111:173848  
GI



AB Linked analogs I [ $X = S(CH_2)_6S$ ,  $OCH_2CH_2NMeCH_2CH_2O$ ] of the DNA binding antibiotic anthramycin are made via nucleophilic arom. substitution of benzoylpyrrolidinecarboxaldehyde deriv. II followed by redn.-cyclization. The linked compds. protect DNA from restriction endonucleases and reversibly crosslink DNA.

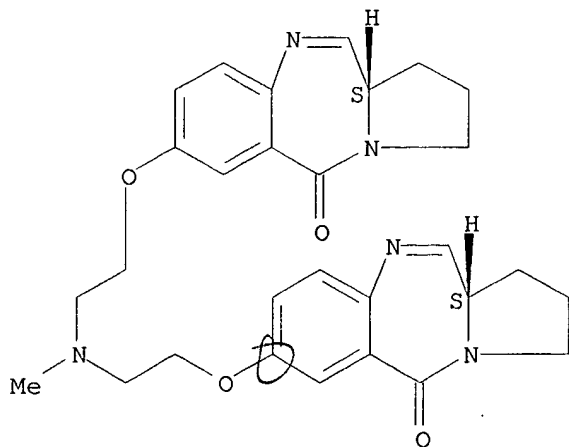
IT **123064-64-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and DNA crosslinking by)

RN 123064-64-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,7'-[(methylimino)bis(2,1-ethanediylloxy)]bis[1,2,3,11a-tetrahydro-, (11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

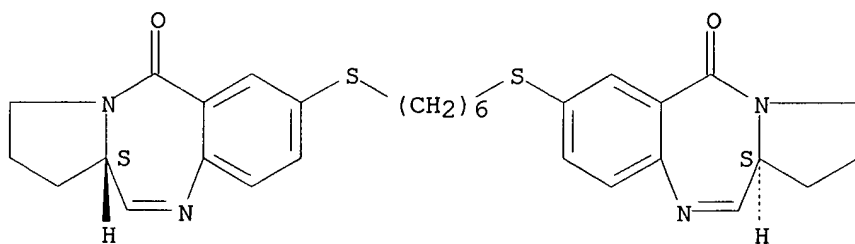
IT **123064-63-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 123064-63-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7,7'-[1,6-hexanediylbis(thio)]bis[1,2,3,11a-tetrahydro-, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

~~126~~ ANSWER 63 OF 107 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1989:93559 CAPLUS

~~DN~~ 110:93559

TI Antitumor antibiotic SF 2364 and its manufacture with Micromonospora

IN Ito, Jiro; Watabe, Hiromi; Ishii, Narutaka; Gomi, Shuichi; Nagasawa, Mieko; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi

PA Meiji Seika Kaisha, Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 10 pp.

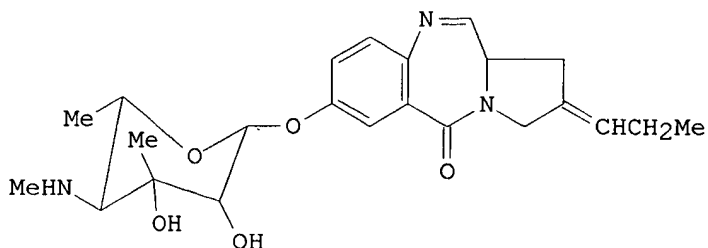
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 63107992	A2	19880512	JP 1986-251887	19861024
GI					



I

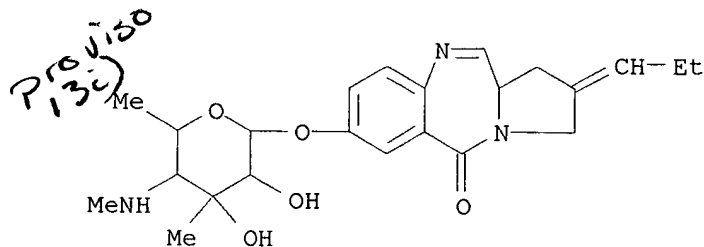
AB Antitumor antibiotic SF2364 (I) is manufd. by cultivating Micromonospora. Micromonospora was cultivated in a 200-L prodn. medium contg. sucrose, wheat germ, salts, etc. at 28.degree. for 3 days with aeration and agitation. The culture filtrate was chromatographed to obtain I.HCl 500 mg.

IT **117782-84-ODP, salts 117782-84-OP 119180-42-6P**

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)  
(manuf. of, with Micromonospora)

RN 117782-84-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-propylidene-, (2E)- (9CI) (CA INDEX NAME)

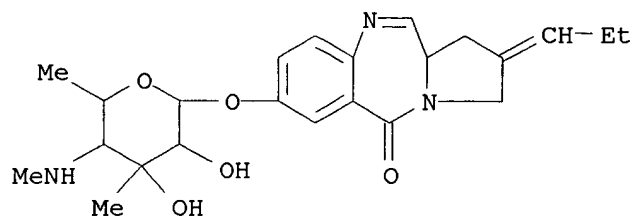


RN 117782-84-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-

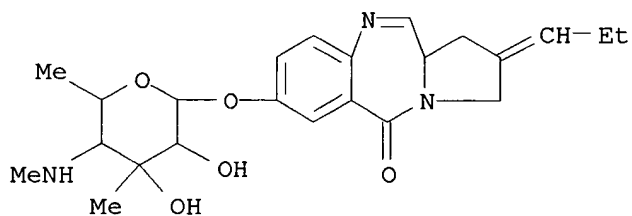
09/763,767

propylidene-, (2E)- (9CI) (CA INDEX NAME)



RN 119180-42-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-propylidene-, monohydrochloride (9CI) (CA INDEX NAME)

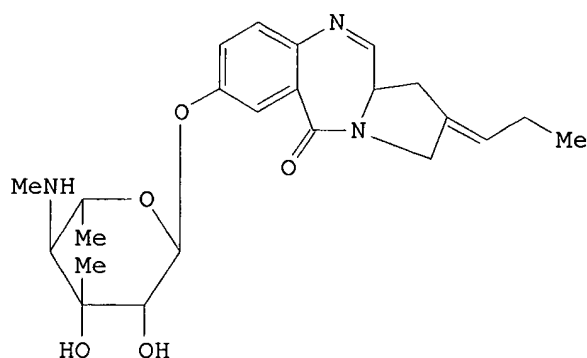


● HCl



09/763,767

~~126~~ ANSWER 64 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1989:4230 CAPLUS  
DN 110:4230  
TI Sibanomicin, a new pyrrolo[1,4]-benzodiazepine antitumor antibiotic  
produced by a Micromonospora sp  
AU Itoh, Jiro; Watabe, Hiroomi; Ishii, Shigetaka; Gomi, Shuichi; Nagasawa,  
Mieko; Yamamoto, Haruo; Shomura, Takashi; Sezaki, Masaji; Kondo, Shinichi  
CS Pharm. Res. Lab., Meiji Seika Kaisha, Ltd., Yokohama, 222, Japan  
SO J. Antibiot. (1988), 41(9), 1281-4  
CODEN: JANTAJ; ISSN: 0021-8820  
DT Journal  
LA English  
GI



I

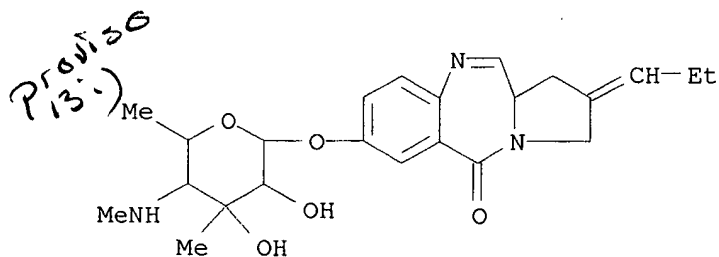
AB The prodn., isolation, characterization, structural elucidation, and biol. properties of a new antibiotic from Micromonospora sp. SF 2364, sibanomicin (I), are reported. The UV spectra of I indicated that it belongs to the anthramycin group. The mol. formula for the hydrochloride of I was C<sub>23</sub>H<sub>31</sub>O<sub>5</sub>.HCl. Whereas the antimicrobial activity of I was very weak, it did show a marked prolongation of the life in mice bearing leukemia P388 cells.

IT **117782-84-0**

RL: BIOL (Biological study)  
(antitumor antibiotic, from Micromonospora)

RN 117782-84-0 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-[[4,6-dideoxy-3-C-methyl-4-(methylamino)-.alpha.-L-mannopyranosyl]oxy]-1,2,3,11a-tetrahydro-2-propylidene-, (2E)- (9CI) (CA INDEX NAME)



~~126~~ ANSWER 65 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1988:621909 CAPLUS

DN 109:221909

TI Pyrrolo[1,4]benzodiazepine antitumor antibiotics: relationship of DNA alkylation and sequence specificity to the biological activity of natural and synthetic compounds

AU Hurley, Laurence H.; Reck, Teri; Thurston, David E.; Langley, David R.; Holden, Kenneth G.; Hertzberg, Robert P.; Hoover, John R. E.; Gallagher, Gregory, Jr.; Faucette, Leo F.; et al.

CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA

SO Chem. Res. Toxicol. (1988), 1(5), 258-68

CODEN: CRTOEC

DT Journal

LA English

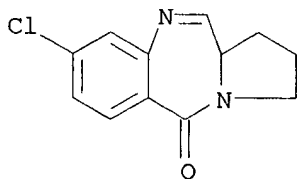
AB The DNA alkylation and sequence specificity of a group of natural and synthetic pyrrolo[1,4]benzodiazepines [P(1,4)Bs] were evaluated by using an exonuclease III stop assay, and the results were compared with in vitro and in vivo biol. potency and antitumor activity. The P(1,4)B antibiotics are potent antitumor agents produced by various Actinomycetes, which are believed to mediate their cytotoxic effects by covalent bonding through N-2 of guanine in the minor groove of DNA. The results of a sensitive DNA alkylation assay using exonuclease III that permits both estn. of the extent of DNA modification as well as location of the precise guanines to which the drugs are covalently bound are described. Using this assay, a series of natural and synthetic compds. of the P(1,4)B class was evaluated for their ability to bond to DNA; also their DNA sequence preference was detd. The compds. included are P(1,4)Bs carrying different substituents in the arom. ring, having varying degrees of satn. in the 5-membered ring, or differing in the stereochem. at C-11a. These same compds. were evaluated for in vitro cytotoxic activity against B16 melanoma cells, for potency in vivo in B6D2F1 mice (LD50), and for antitumor activity (ILSmax) against P388 leukemia cells. A good correlation was found between extent of DNA bonding and in vitro and in vivo potency. Furthermore, on the basis of electronic and steric considerations, it was possible to rationalize why those compds. that showed negligible biol. activity were unable to bond covalently to DNA. The degree of satn. in the five-membered ring of the P(1,4)Bs had a significant effect on the DNA bonding reactivity and biol. activity of this class of compds.

IT 116564-84-2P 116564-97-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 116564-84-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 8-chloro-1,2,3,11a-tetrahydro-  
(9CI) (CA INDEX NAME)

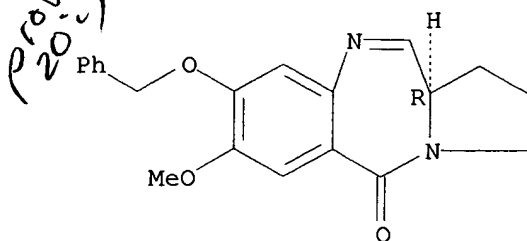


RN 116564-97-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methoxy-  
8-(phenylmethoxy)-, (R)- (9CI) (CA INDEX NAME)

09/763,767

Provisional  
Absolute stereochemistry.



09/763,767

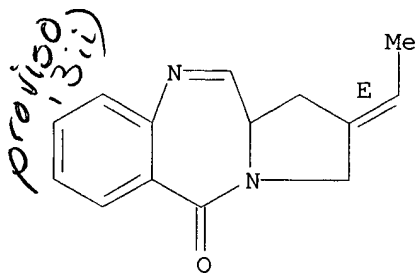
~~IX~~ 6 ANSWER 66 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1988:492593 CAPLUS  
DN 109:92593  
TI The total synthesis of DC-81, a pyrrolo[1,4]benzodiazepine antitumor  
antibiotic  
AU Weidner, Michele Ann  
CS Univ. Maryland, College Park, MD, USA  
SO (1987) 245 pp. Avail.: Univ. Microfilms Int., Order No. DA8725588  
From: Diss. Abstr. Int. B 1988, 48(8), 2328-9  
DT Dissertation  
LA English  
AB Unavailable  
IT **89824-22-6P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(total synthesis of)  
RN 89824-22-6 CAPLUS

*Proviso  
20.7*

09/763,767

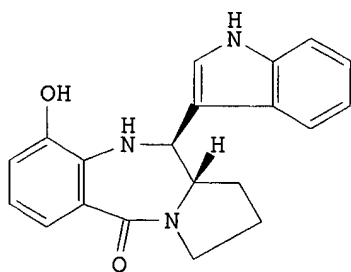
~~LP~~ 6 ANSWER 67 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1987:598720 CAPLUS  
DN 107:198720  
TI New synthesis of heterocycles by use of organometallic complexes: the application to the syntheses of biologically active substances  
AU Mori, Miwako  
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan  
SO Yakugaku Kenkyu no Shinpo (1986), 2, 127-50  
CODEN: YAKSEY  
DT Journal  
LA Japanese  
AB A symposium on the formation of 1,4-benzodiazepine skeleton from o-haloanilines and amino acids via palladium catalyzed carbonylation. The total syntheses of anthramycin, prothracarcin, tomaymycin, SEN-215, and neothramycin, which were antitumor antibiotics were achieved in good overall yields from l-proline or 4-hydroxy-l-proline as amino acid. A one step synthesis of quinazolines from o-haloanilines and five membered lactams or primary amines was developed by use of palladium catalyzed carbonylation. Though the alkylmetal complex could not be synthesized from the alkyl halide, .alpha.-halocarbonyl compds. such as .alpha.-halo amides, .alpha.-halo esters, .alpha.-halo ketones, and .alpha.-halo nitriles having internal double bonds were treated with Pd(PPh<sub>3</sub>)<sub>4</sub> to afford the cyclized products in good yields presumably through the .sigma.-alkylmetal complex. By use of this method, pyrrolizidine alkaloids and oxacepham skeleton were synthesized.  
IT **105498-29-1P**, (.+-.)-Prothracarcin  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(total synthesis of)  
RN 105498-29-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

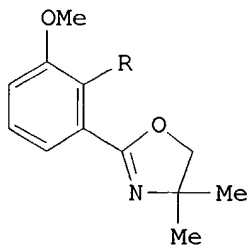


09/763,767

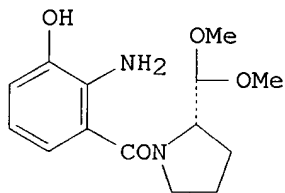
~~LN~~ 6 ANSWER 68 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~IN~~ 1987:575731 CAPLUS  
DN 107:175731  
TI Stereoselective total synthesis of tilivalline  
AU Mori, Shigehiro; Aoyama, Toyohiko; Shioiri, Takayuki  
CS Fac. Pharm. Sci., Nagoya City Univ., Japan  
SO Tennen Yuki Kagobutsu Toronkai Koen Yoshishu (1986), 28th, 481-7  
CODEN: TYKYDS  
DT Journal  
LA Japanese  
GI



I



II



IV

AB Stereoselective synthesis of tilivalline (I) is described. Oxazoline II (R = H) was aminated to give II (R = NH<sub>2</sub>) which was hydrolyzed with HCl in the presence of red P to give m-hydroxyanthranilic acid (III). Condensation of III with L-prolinal dimethylacetal hydrochloride by the (EtO)<sub>2</sub>P(O)CN afforded the amide IV. Successive treatment of IV with Me<sub>3</sub>SiCl, and NaI in pyridine, followed by indole, and ZnCl<sub>2</sub> in a one-pot process gave I in excellent yield.

IT **110715-89-4P**

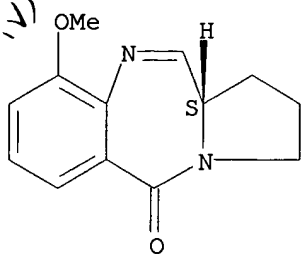
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 110715-89-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

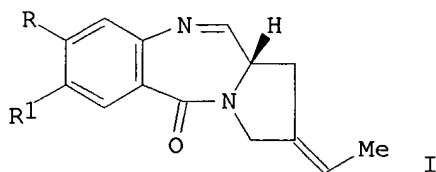
Absolute stereochemistry.

05/11/2015



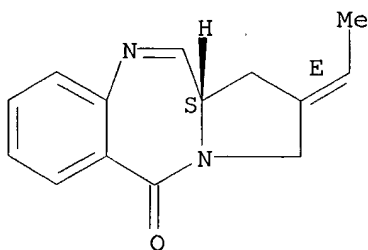
09/763,767

~~126~~ ANSWER 69 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1987:458707 CAPLUS  
DN 107:58707  
TI Total syntheses of prothracarcin and tomaymycin by use of palladium  
catalyzed carbonylation  
AU Mori, Miwako; Uozumi, Yasuhiro; Kimura, Masaya; Ban, Yoshio  
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan  
SO Tetrahedron (1986), 42(14), 3793-806  
CODEN: TETRAB; ISSN: 0040-4020  
DT Journal  
LA English  
OS CASREACT 107:58707  
GI



AB Total synthesis of optically active prothracarcin (I, R = R1 = H) and  
pretomaymycin (I, R = OH, R1 = OMe), which is readily convertible to  
tomaymycin, were achieved via a Pd-catalyzed carbonylation. The structure  
of prothracarcin was detd. to be (11aS)(E)-I (R = R1 = H) by comparison of  
the <sup>13</sup>C-NMR spectra of the synthetic E- and Z-isomers.  
IT **81542-99-6P**, Prothracarcin  
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and mol. structure of)  
RN 81542-99-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-  
tetrahydro-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

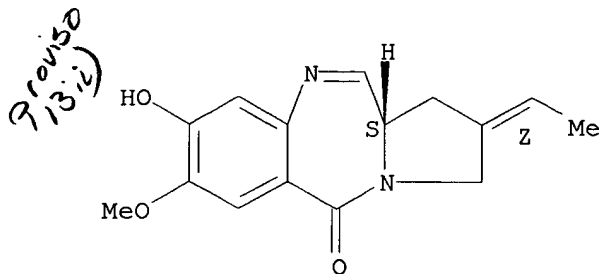


IT **81422-29-9P 81422-30-2P**, Pretomaymycin  
**105120-29-4P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 81422-29-9 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-  
tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)



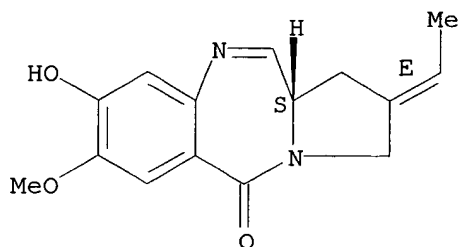
09/763,767

Absolute stereochemistry.  
Double bond geometry as shown.



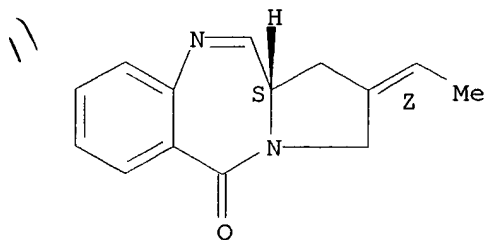
RN 81422-30-2 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



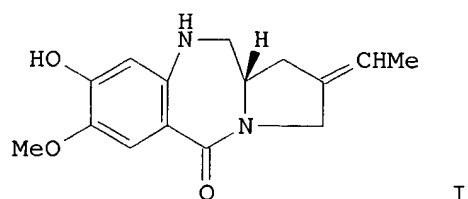
RN 105120-29-4 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



09/763,767

~~LI~~6 ANSWER 70 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1987:84241 CAPLUS  
DN 106:84241  
TI Structure and syntheses of SEN-215 and oxotomaymycin  
AU Mori, Miwako; Uozumi, Yasuhiro; Ban, Yoshio  
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan  
SO Heterocycles (1986), 24(5), 1257-60  
CODEN: HTCYAM; ISSN: 0385-5414  
DT Journal  
LA English  
OS CASREACT 106:84241  
GI



AB The structure of SEN-215 was detd. as (11aS) (E)-2-ethylidene-2,3,5,10,11,11a-hexahydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepine (I) by conversion of (E)- and (Z)-pretomaymycin into (E)- and (Z)-I.

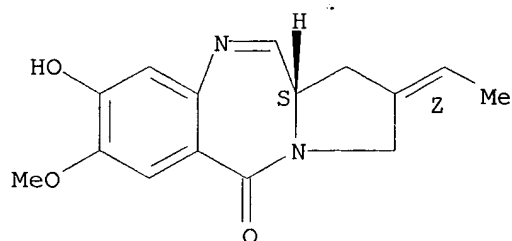
IT **81422-29-9P 81422-30-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and redn. of)

RN 81422-29-9 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

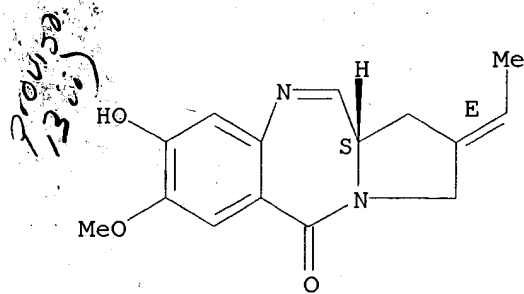


RN 81422-30-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

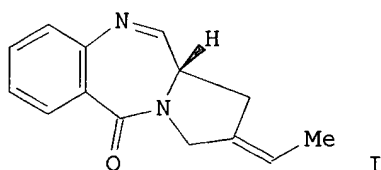
Absolute stereochemistry.  
Double bond geometry as shown.

09/763,767



09/763,767

~~L26~~ ANSWER 71 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~RN~~ 1987:66984 CAPLUS  
DN 106:66984  
TI A versatile and efficient synthesis of carbinolamine-containing  
pyrrolo[1,4]benzodiazepines via the cyclization of N-(2-  
aminobenzoyl)pyrrolidine-2-carboxaldehyde diethyl thioacetals: total  
synthesis of prothracarcin  
AU Langley, David R.; Thurston, David E.  
CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA  
SO J. Org. Chem. (1987), 52(1), 91-7  
CODEN: JOCEAH; ISSN: 0022-3263  
DT Journal  
LA English  
OS CASREACT 106:66984  
GI



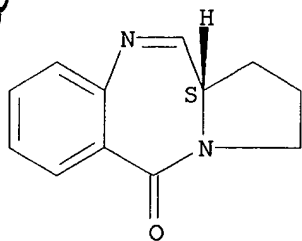
AB A versatile and efficient synthesis of carbinolamine-contg.  
pyrrolo[1,4]benzodiazepines (or the corresponding imine forms) is  
described that involves HgCl<sub>2</sub>-mediated cyclization of the corresponding  
N-(2-aminobenzoyl)pyrrolidine-2-carboxaldehyde di-Et thioacetals. This  
new synthesis has significant advantages over previously existing methods  
in that (a) catalytic hydrogenation is not involved in the cyclization  
process, thus allowing preservation of unsatn. in the product, (b) all  
steps are mild and take place in high yields, (c) the success of the  
reaction is apparently independent of substituent effects, (d) the  
reaction proceeds with retention of stereochem. at the aldehyde bearing  
carbon, and (e) it can be readily adapted for the convergent synthesis of  
a variety of analogs. In addn. to the synthesis of some model  
carbinolamine-contg. compds., the overall utility of this procedure is  
demonstrated by the total synthesis of prothracarcin (I), a natural  
product with antitumor activity from Streptomyces umbrosus. This allowed  
confirmation of the E configuration previously assigned to the  
C2-ethylidene side chain of I.

IT **72435-89-3P 100231-11-6P 100231-12-7P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

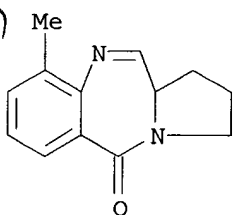
09/763,767

Proviso  
c1, 20



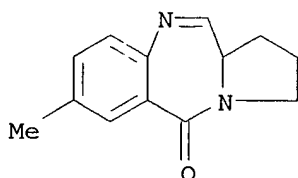
RN 100231-11-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methyl-  
(9CI) (CA INDEX NAME)

Proviso  
20 (12)



RN 100231-12-7 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl-  
(9CI) (CA INDEX NAME)

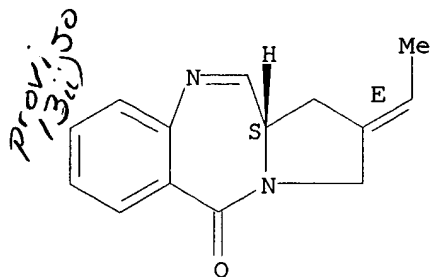
11



IT **81542-99-6P**, Prothracarcin **105120-29-4P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(total synthesis of)  
RN 81542-99-6 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-  
tetrahydro-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

09/763,767

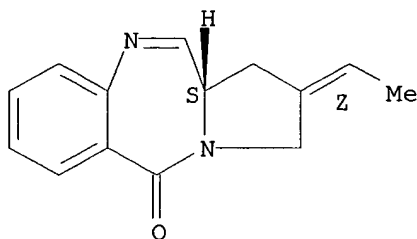


RN 105120-29-4 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

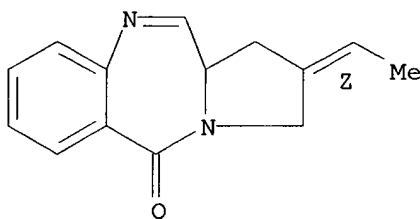
Double bond geometry as shown.



09/163,767

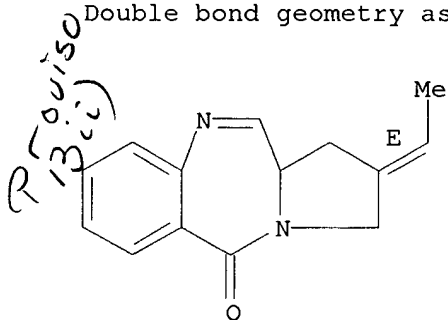
~~126~~ ANSWER 72 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1986:627189 CAPLUS  
DN 105:227189  
TI Part I. The total synthesis of the pyrrolo(1,4)benzodiazepines E and Z-prothracarcin. Part II. Carbohydrate-based approaches to the C33-37 portion of amphotericin B  
AU Schuda, Ann DeCamp  
CS Univ. Maryland, College Park, MD, USA  
SO (1985) 238 pp. Avail.: Univ. Microfilms Int., Order No. DA8604216  
From: Diss. Abstr. Int. B 1986, 46(12), Pt. 1, 4249-50  
DT Dissertation  
LA English  
AB Unavailable  
IT **105498-28-0P 105498-29-1P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(total synthesis of)  
RN 105498-28-0 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



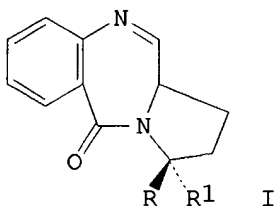
RN 105498-29-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



09/763,767

~~E26~~ ANSWER 73 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1986:572417 CAPLUS  
DN 105:172417  
TI A one step synthesis of 1,4-benzodiazepines: synthetic studies on  
neothramycin  
AU Mori, Miwako; Kimura, Masaya; Uozumi, Yasuhiro; Ban, Yoshio  
CS Fac. Pharm. Sci., Hokkaido Univ., Sapporo, 060, Japan  
SO Tetrahedron Lett. (1985), 26(48), 5947-50  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 105:172417  
GI



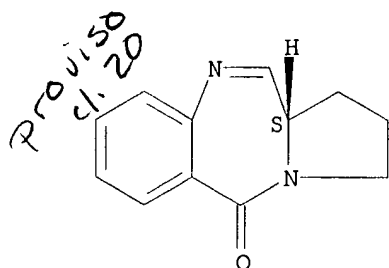
AB A one step synthesis of 1,4-benzodiazepines from o-haloanilines and amino acids was achieved by use of palladium catalyzed carbonylation, by which application a synthesis of the model compds. I (R = MeO, R1 = H; R = H; R1 = MeO) of Neothramycin (A and B) was described. An efficient chemoselective redn. of the amide was provided.

IT **72435-89-3P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 72435-89-3 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

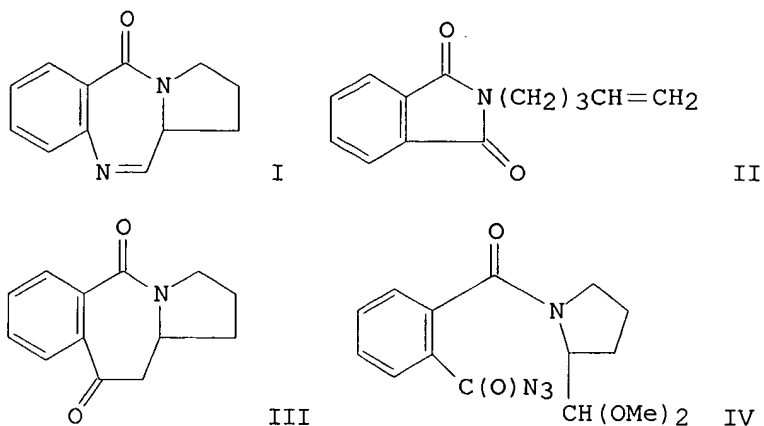
Absolute stereochemistry. Rotation (+).





09/763,767

~~126~~ ANSWER 74 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1986:406496 CAPLUS  
DN 105:6496  
TI A photochemical route to pyrrolo[1,4]benzodiazepine antitumor antibiotics  
AU Mazzocchi, Paul H.; Schuda, Ann DeCamp  
CS Dep. Chem., Univ. Maryland, College Park, MD, 20742, USA  
SO Heterocycles (1985), 23(7), 1603-6  
CODEN: HTCYAM; ISSN: 0385-5414  
DT Journal  
LA English  
OS CASREACT 105:6496  
GI

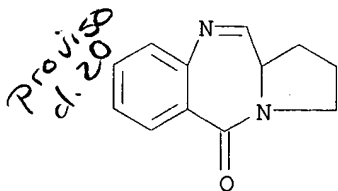


AB The ketone I, contg. the title ring system, was prepd. in a sequence involving the photochem. ring expansion of the phthalimide II to the dioxopyrrolobenzazepine III and a Curtius rearrangement of a ring opened III derived compd. IV.

IT **102609-85-8P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

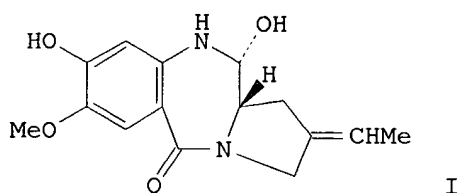
RN 102609-85-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro- (9CI)  
(CA INDEX NAME)



09/763,767

~~L26~~ ANSWER 75 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1986:199669 CAPLUS  
DN 104:199669  
TI Pyrrolo[1,4]benzodiazepine antitumor antibiotics: evidence for two forms of tomaymycin bound to DNA  
AU Barkley, Mary D.; Cheatham, Steve; Thurston, David E.; Hurley, Laurence H.  
CS Med. Cent., Univ. Kentucky, Lexington, KY, 40536, USA  
SO Biochemistry (1986), 25(10), 3021-31  
CODEN: BICHAW; ISSN: 0006-2960  
DT Journal  
LA English  
GI



AB Two fluorescent ground-state species of tomaymycin (I), an antibiotic belonging to the pyrrolo[1,4]benzodiazepine group of antitumor compds., were obsd. in protic solvents and in its adducts with DNA; 1H NMR studies showed that the 2 fluorescent species in MeOH were the 11R,11aS-[35050-55-6] and 11S,11aS-11-Me ether of tomaymycin [101313-08-0]. On the basis of epimerization expts. and exchange of 13C from 13MeOH into the C-11 methoxy group of the tomaymycin Me ether, a mechanism is proposed for their interconversion via 10,11-anhydrotomaymycin [81422-30-2]. Coupling information revealed that the soln. conformations of the 2 diastereomers differ, with the C-5 carbonyl lying closer to the plane of the arom. ring in the 11R,11aS diastereomer. The fluorescence excitation and emission spectra of the 2 emitting species in MeOH were sepd. by time-resolved fluorescence spectroscopy and were assocd. with the diastereomeric forms identified by 1H NMR. Time-resolved fluorescence studies of tomaymycin in protic solvents and on DNA indicated that the absorption spectrum of the longer lifetime component (11R,11aS form) is red-shifted relative to the absorption spectrum of the shorter lifetime component (11S,11aS form), consistent with more extensive conjugation. The 2 conformational forms of tomaymycin on DNA were tentatively identified as the 11S,11aS and 11R,11aS diastereomeric adducts, which bind in opposite orientations in the minor groove. This proposal is supported by mol. modeling studies with the use of a hexamer adduct of d(ATGCAT)2.

IT **81422-30-2**

RL: BIOL (Biological study)

(tomaymycin Me ether epimerization mechanism in relation to)

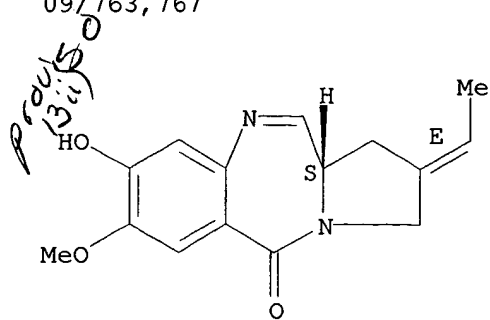
RN 81422-30-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

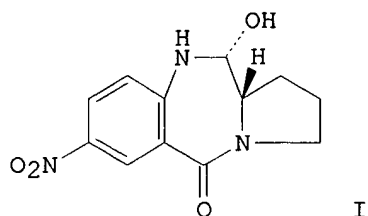
Double bond geometry as shown.

09/763,767



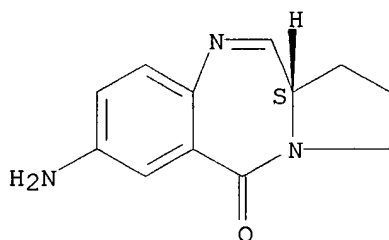
09/763,767

L26 ANSWER 76 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1986:168234 CAPLUS  
DN 104:168234  
TI Synthesis and structure of anthramycin analogs via hydride reduction of  
dilactams  
AU Suggs, J. William; Wang, Yueh Sha; Lee, Ken S.  
CS Dep. Chem., Brown Univ., Providence, RI, 02912, USA  
SO Tetrahedron Lett. (1985), 26(40), 4871-4  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
OS CASREACT 104:168234  
GI



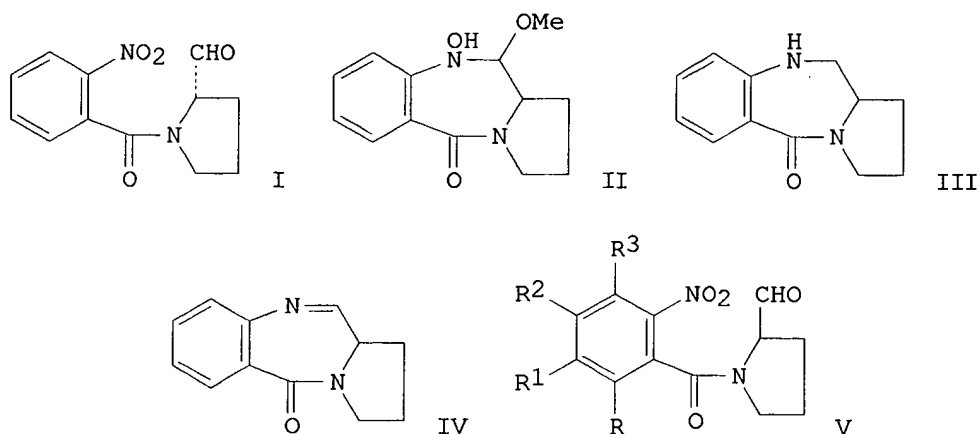
AB Hydride redn. of pyrrolo[1,4]benzodiazepin-5,10-diones to carbinolamines  
is possible if a sufficiently electron-withdrawing group, such as NO<sub>2</sub>, is  
present on the arom. ring. The x-ray structure of one such product, I, is  
given.  
IT **101664-41-9P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and quaternization of)  
RN 101664-41-9 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 7-amino-1,2,3,11a-tetrahydro-,  
(S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

✓  
126 ANSWER 77 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1986:129877 CAPLUS  
DN 104:129877  
TI Synthesis and stereochemistry of carbinolamine-containing  
pyrrolo[1,4]benzodiazepines by reductive cyclization of  
N-(2-nitrobenzoyl)pyrrolidine-2-carboxaldehydes  
AU Thurston, David E.; Langley, David R.  
CS Coll. Pharm., Univ. Texas, Austin, TX, 78712, USA  
SO J. Org. Chem. (1986), 51(5), 705-12  
CODEN: JOCEAH; ISSN: 0022-3263  
DT Journal  
LA English  
OS CASREACT 104:129877  
GI



AB Products from the reductive cyclization (H, Pd/C) of the aldehyde (S)-I varied with time and other conditions; typical products were the carbinolamine II and the amine III, but in no case was the earlier reported ketone IV obtained. Reductive cyclization of the racemic aldehydes V (R, R1, R2, R3 = H, H, Me, OH; H, H, H, Me; H, Me, H, H; Me, H, H, H; H, H, H, MeO) was also studied under a variety of conditions.

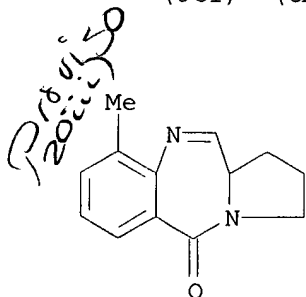
IT 100231-11-6P 100231-12-7P 100231-13-8P

100231-14-9P 100296-65-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

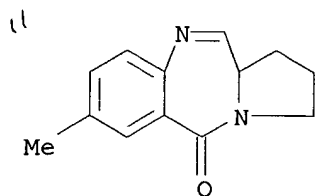
RN 100231-11-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methyl-  
(9CI) (CA INDEX NAME)

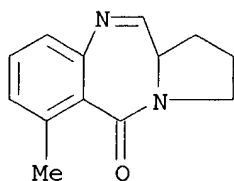


09/763,767

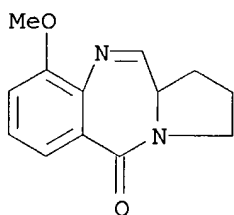
RN 100231-12-7 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-7-methyl-  
(9CI) (CA INDEX NAME)



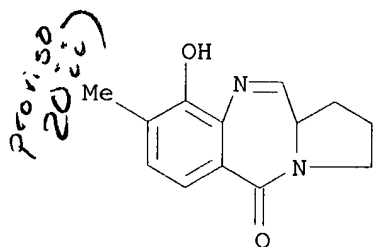
RN 100231-13-8 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-6-methyl-  
(9CI) (CA INDEX NAME)



RN 100231-14-9 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-methoxy-  
(9CI) (CA INDEX NAME)



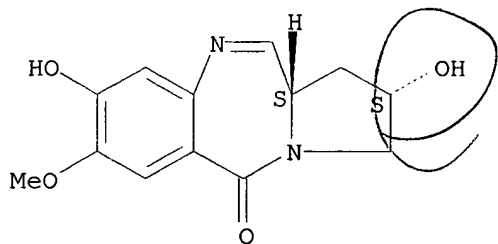
RN 100296-65-9 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-  
8-methyl- (9CI) (CA INDEX NAME)



09/763,767

~~126~~ ANSWER 78 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1984:468945 CAPLUS  
DN 101:68945  
TI Chicamycin, a new antitumor antibiotic. I. Production, isolation and properties  
AU Konishi, Masataka; Hatori, Masami; Tomita, Koji; Sugawara, Masaru; Ikeda, Chiharu; Nishiyama, Yuji; Imanishi, Hideyo; Miyaki, Takeo; Kawaguchi, Hiroshi  
CS Bristol-Banyu Res. Inst., Ltd., Tokyo, Japan  
SO J. Antibiot. (1984), 37(3), 191-9  
CODEN: JANTAJ; ISSN: 0021-8820  
DT Journal  
LA English  
AB Chicamycin is a new antitumor antibiotic produced by a strain of *Streptomyces albus*, no. J576-99. The antibiotic is extractable into org. solvents from the fermn. broth and is obtained in 2 active forms, chicamycins A and B; the form depends upon the isolation procedure used. Chicamycin A is not a natural antibiotic but the MeOH adduct of naturally produced chicamycin B. Both forms of the antibiotic have weak antibacterial activity against some gram-pos. and acid-fast bacteria. They inhibit the growth of exptl. tumors, such as P388 mouse leukemia.  
IT **89675-39-8**  
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (from *Streptomyces albus*, antitumor activity of)  
RN 89675-39-8 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

126 ANSWER 79 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1984:420267 CAPLUS

DN 101:20267

TI Chicamycin, a new antitumor antibiotic. II. Structure determination of chicamycins A and B

AU Konishi, Masataka; Ohkuma, Hiroaki; Naruse, Nobuaki; Kawaguchi, Hiroshi

CS Bristol-Banyu Res. Inst., Ltd., Tokyo, Japan

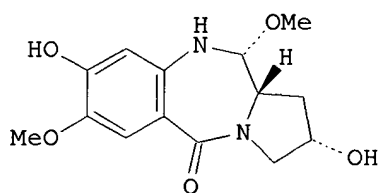
SO J. Antibiot. (1984), 37(3), 200-6

CODEN: JANTAJ; ISSN: 0021-8820

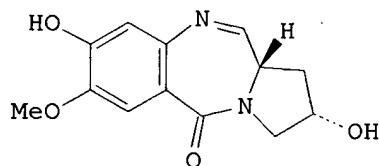
DT Journal

LA English

GI



I



II

AB Structures of chicamycins A (I) and B (II) were detd. from a series of chem. degrading studies coupled with spectroscopic anal. The structure of II is closely related to neothramycin, differing only in the position of a hydroxyl substituent on the pyrrolidine ring.

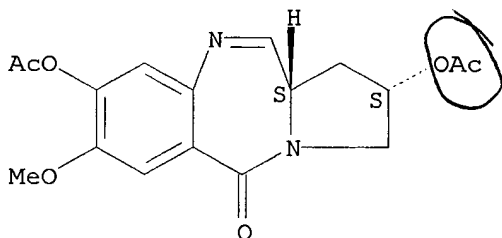
IT 90569-56-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 90569-56-5 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2,8-bis(acetyloxy)-1,2,3,11a-tetrahydro-7-methoxy-, (2S-trans)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 89675-39-8

RL: PRP (Properties)

(structure of, antitumor antibiotic activity in relation to)

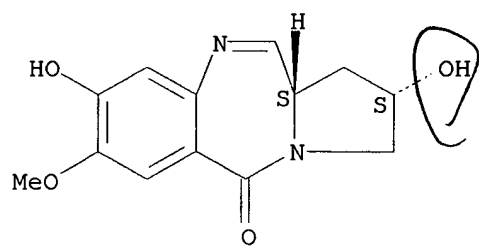
RN 89675-39-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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126 ANSWER 80 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1984:405551 CAPLUS

DN 101:5551

TI Antitumor antibiotics

IN Hatori, Masami; Ohkuma, Hiroaki; Konishi, Masataka; Miyaki, Takeo;  
Kawaguchi, Hiroshi

PA Bristol-Myers Co. , USA

SO Eur. Pat. Appl., 53 pp.

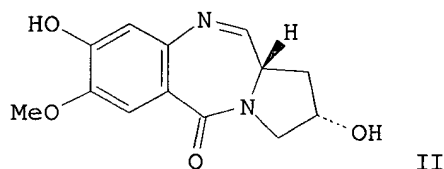
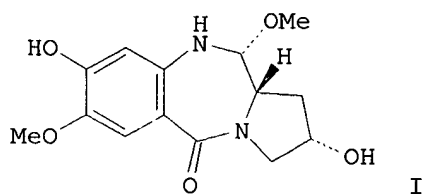
CODEN: EPXXDW

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 101924	A1	19840307	EP 1983-107303	19830725
	EP 101924	B1	19880921		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	US 4464467	A	19840807	US 1982-401469	19820726
	CA 1213542	A1	19861104	CA 1983-430626	19830617
	AT 37394	E	19881015	AT 1983-107303	19830725
	JP 59036678	A2	19840228	JP 1983-135283	19830726
	JP 05021909	B4	19930325		
	US 4508647	A	19850402	US 1984-608736	19840510
	JP 05076350	A2	19930330	JP 1991-305643	19911025
PRAI	US 1982-401469		19820726		
	EP 1983-107303		19830725		
GI					



AB Two new antibiotics, designated BBM-2040A (I) [89675-37-6] and BBM-2040B (II) [89675-39-8], are produced by aerobic fermn. of Streptomyces species strain J576-99 in a medium contg. 3% soybean meal, 2% corn starch, 1% CaCO<sub>3</sub>, and 0.33% MgSO<sub>4</sub>·7H<sub>2</sub>O, pH 7.0, at 28.degree. for 120 h. I was isolated from the culture filtrate by extn. with MeOH and purified by column chromatog. II was isolated by extn. with a nonmethanolic solvent such as BuOH, followed by column chromatog. and TLC at 5.degree.. Both I and II were recovered in their desmethanol or methanol adduct form. The yields of I and II were 1.10 and 3.30 g, resp. The antibiotics inhibited gram-pos. and acid-fast bacteria and slowed the growth of tumors such as P388 leukemia in mice.

IT 89675-39-8

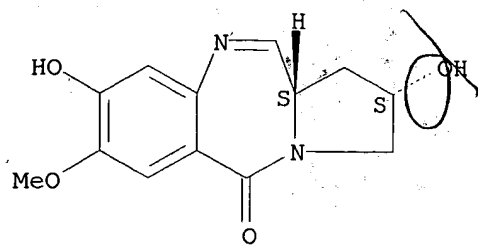
RL: BIOL (Biological study)  
(antitumor antibiotic, from Streptomyces)

RN 89675-39-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

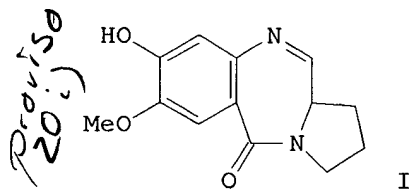
09/763,767



09/763,767

~~126~~ ANSWER 81 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1984:173150 CAPLUS  
DN 100:173150  
TI Antibiotic DC-81  
PA Kyowa Hakko Kogyo Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 9 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 58180487	A2	19831021	JP 1982-63630	19820416
GI					



AB Antibiotic DC-81 (I) [89824-22-6] is isolated from cultures of *Streptomyces roseiscleroticus* DC-81. Thus, the microorganism was cultured at 30.degree. for 72 h on a medium contg. dextrin 50, soybean meal 20, KH<sub>2</sub>PO<sub>4</sub> 0.5, MgSO<sub>4</sub>.7H<sub>2</sub>O 0.5, and CaCO<sub>3</sub> 5 g/L and filtered.

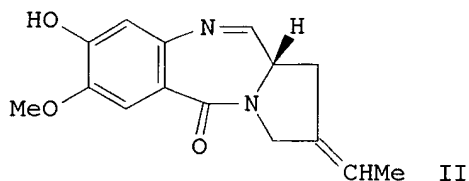
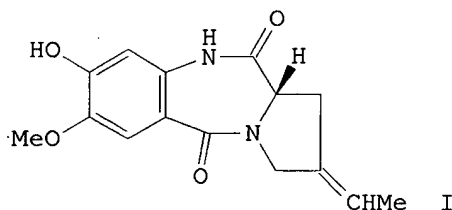
IT **89824-22-6**  
RL: BIOL (Biological study)  
(antibiotic, from *Streptomyces roseiscleroticus*)

RN 89824-22-6 CAPLUS

09/763,767

~~D26~~ ANSWER 82 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1984:156434 CAPLUS  
DN 100:156434  
TI Conversion of oxotomaymycin to tomaymycin  
IN Kaneko, Takushi; Wong, Henry S. L.  
PA Bristol-Myers Co. , USA  
SO U.S., 8 pp.  
CODEN: USXXAM  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4427588	A	19840124	US 1982-439965	19821108
	JP 59101486	A2	19840612	JP 1983-208436	19831108
	JP 05024157	B4	19930406		
PRAI	US 1982-439965		19821108		
GI					



AB Oxotomaymycin (I) was converted to demethanoltomaymycin (II) by benzoylation, thiolation, S-methylation, methoxylation of the methylthio deriv., redn. of the imino ether bond, and elimination of MeOH.

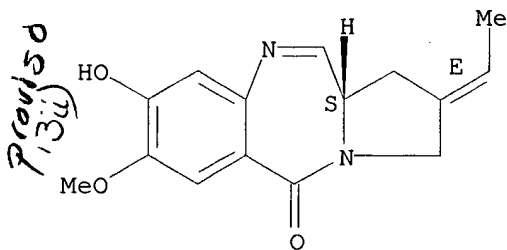
IT **81422-30-2P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 81422-30-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



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~~126~~ ANSWER 83 OF 107 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1984:156433 CAPLUS

DN 100:156433

TI Total synthesis of antitumor antibiotics BBM-2040A and BBM-2040B

IN Kaneko, Takushi; Wong, Henry S. L.

PA Bristol-Myers Co. , USA

SO U.S., 23 pp.

CODEN: USXXAM

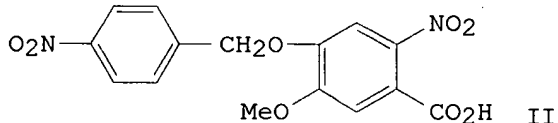
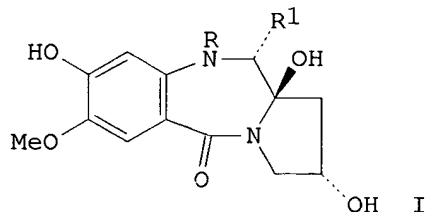
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4427587	A	19840124	US 1982-440779	19821110
	EP 109047	A1	19840523	EP 1983-111195	19831109
	EP 109047	B1	19871104		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	AT 30591	E	19871115	AT 1983-111195	19831109
	JP 59101487	A2	19840612	JP 1983-210023	19831110
	JP 05016430	B4	19930304		
	JP 05247046	A2	19930924	JP 1992-88431	19920227
	JP 07020962	B4	19950308		
PRAI	US 1982-440779		19821110		
	EP 1983-111195		19831109		

GI



AB The title compds. I (R = H, R1 = OMe; RR1 = bond) were prepd. from trans-4-hydroxy-L-proline and benzoic acid II in 9 steps. I had significant antitumor activity at 3 mg/kg day i.p. in mice.

IT **89675-39-8P**

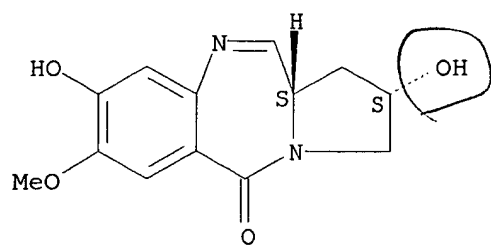
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. and antitumor activity of)

RN 89675-39-8 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

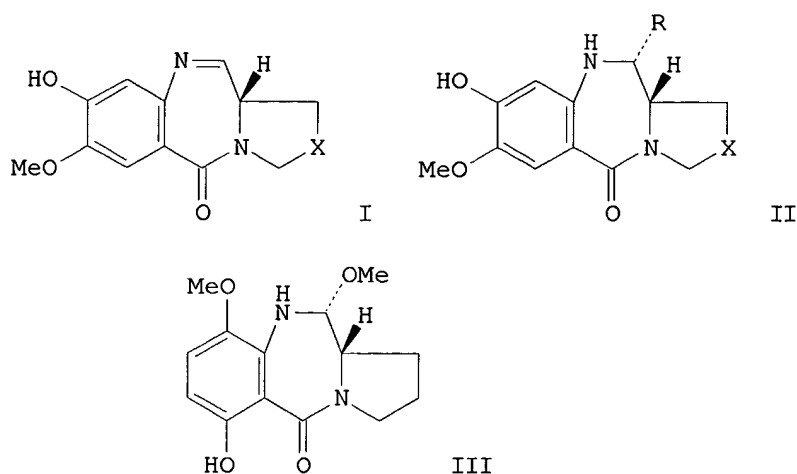
09/763,767



see 8909107

09/763,767

DI 6 ANSWER 84 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1984:138816 CAPLUS  
DN 100:138816  
TI Studies on tomaymycin. III. Syntheses and antitumor activity of  
tomaymycin analogs  
AU Tozuka, Zenzaburo; Yazawa, Hisatoyo; Murata, Masayoshi; Takaya, Takao  
CS Res. Lab., Fujisawa Pharm. Co., Ltd., Osaka, Japan  
SO J. Antibiot. (1983), 36(12), 1699-708  
CODEN: JANTAJ; ISSN: 0021-8820  
DT Journal  
LA English  
GI



AB Analogs I-III [X = CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, S, CHOH, CO, CHO<sub>2</sub>C(CH<sub>2</sub>)<sub>14</sub>Me, CO, C:NOMe, C:CHCN, C:CHMe; R = OMe, NEt<sub>2</sub>, SEt, SCH<sub>2</sub>Ph] of tomaymycin (II, X = C:CHMe, R = OMe) were prepd. Most of them were inactive against leukemia P388 in mice and the activity of the others was less than that of tomaymycin. Only the O-Me deriv. of tomaymycin had antileukemic activity comparable to that of the parent.

IT 85993-77-7

RL: BAC (Biological activity or effector, except adverse); BIOL  
(Biological study)  
(antitumor activity of)

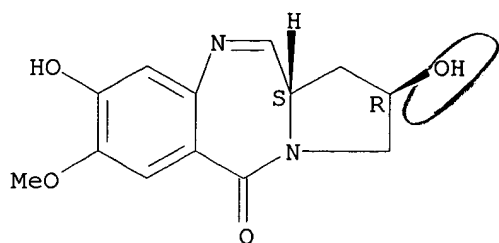
RN 85993-77-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2R-cis)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767



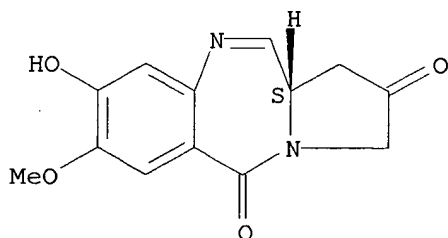
IT 81306-73-2P 81307-24-6P 89300-07-2P  
89300-08-3P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. and antitumor activity of)

RN 81306-73-2 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione, 8-hydroxy-7-methoxy-, (S)- (9CI) (CA INDEX NAME)

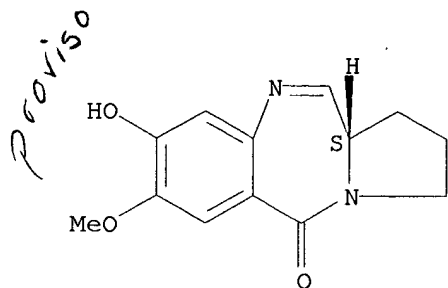
Absolute stereochemistry.



RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



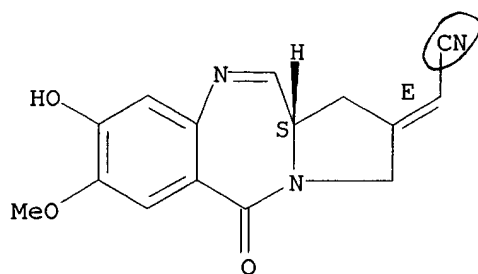
RN 89300-07-2 CAPLUS

CN Acetonitrile, (5,11a-dihydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene)-, [S-(E)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

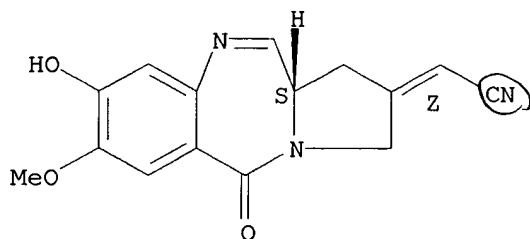
09/763,767



RN 89300-08-3 CAPLUS

CN Acetonitrile, (5,11a-dihydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene)-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



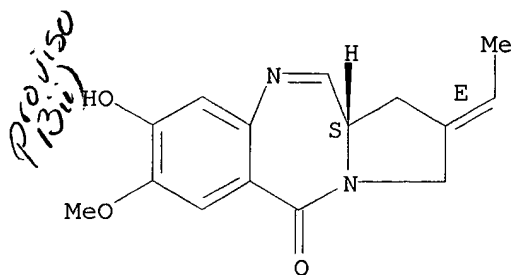
IT 81422-30-2

RL: RCT (Reactant)  
(reaction of, with thiols)

RN 81422-30-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

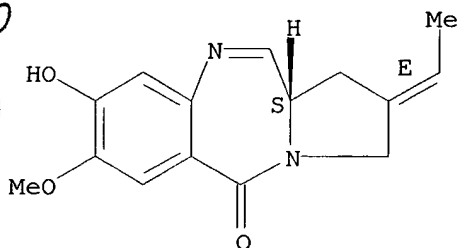
Absolute stereochemistry.  
Double bond geometry as shown.



09/763,767

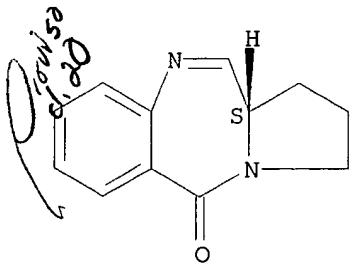
~~126~~ ANSWER 85 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1984:138814 CAPLUS  
~~DN~~ 100:138814  
TI A new and mild method for the reduction of secondary amides to carbinolamine ethers and imines: a conversion of oxotomaymycin to tomaymycin  
AU Kaneko, T.; Wong, H.; Doyle, T. W.  
CS Pharm. Res. Dev. Div., Bristol-Myers Co., Syracuse, NY, 13221-4755, USA  
SO Tetrahedron Lett. (1983), 24(47), 5165-8  
CODEN: TELEAY; ISSN: 0040-4039  
DT Journal  
LA English  
AB Secondary carboxamides were reduced to the corresponding amines by thiolation, iminoalkylation, and Al-Hg redn. of the intermediate thiol ethers. Thus, oxotomaymycin was converted to the thione, S-methylated, and reduced with AlHg in aq. THF to give pretomaymycin which was methanolized with MeOH at <0.degree. to give tomaymycin (I).  
IT **81422-30-2P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and methanolysis of)  
RN 81422-30-2 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



IT **72435-89-3P**  
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)  
RN 72435-89-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



09/763,767

126 ANSWER 86 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1983:539984 CAPLUS

DN 99:139984

TI Benzodiazepine derivatives

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 7 pp.

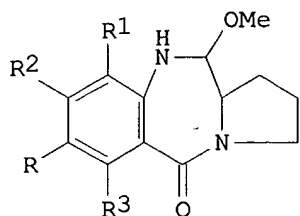
CODEN: JKXXAF

DT Patent

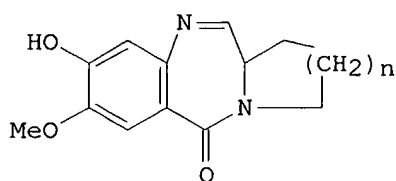
LA Japanese

FAN.CNT 1

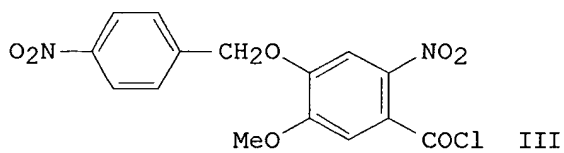
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 58041878	A2	19830311	JP 1981-141503	19810907
GI					



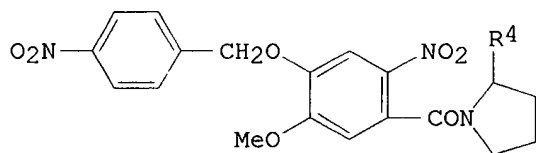
I



II



III



IV

AB I (R-R3 = MeO, H, OH, H; H, MeO, H, OH) and II (n = 1,2) were prepd. and tested for anticarcinogenic activity on mouse leukemia cells P388. Thus, condensation of III with L-proline in THF contg. Et3N at room temp. gave IV (R4 = CO2H), hydride redn. gave IV (R4 = CHO), and hydrogenolysis in MeOH-EtOAc contg. Pd/BaSO4 at room temp. for 4 h gave I (R-R3 = MeO, H, OH, H) and II (n = 1).

IT 81307-24-6P

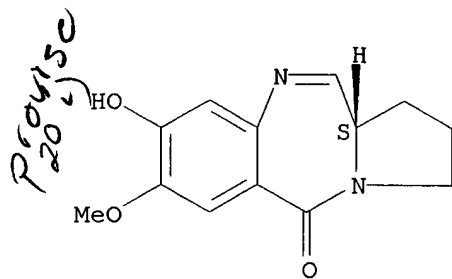
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and antileukemia activity of)

RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

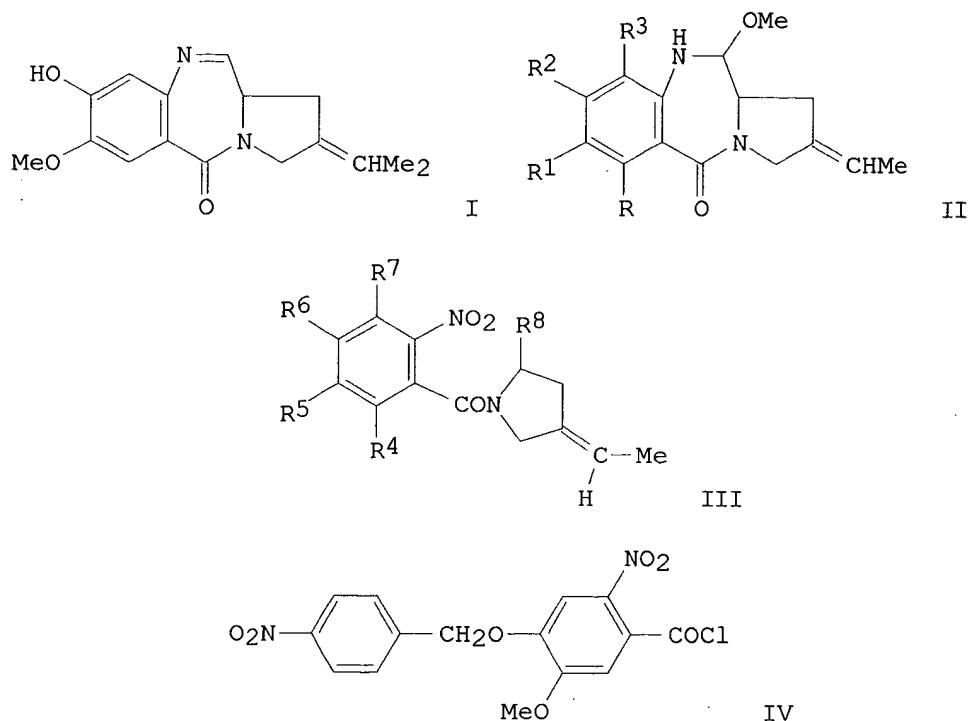
09/763,767



09/763,767

L26 ANSWER 87 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1983:539983 CAPLUS  
 DN 99:139983  
 TI Benzodiazepine derivatives  
 PA Fujisawa Pharmaceutical Co., Ltd., Japan  
 SO Jpn. Kokai Tokkyo Koho, 10 pp.  
 CODEN: JKXXAF  
 DT Patent  
 LA Japanese  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 58041884	A2	19830311	JP 1981-141502	19810907
GI					



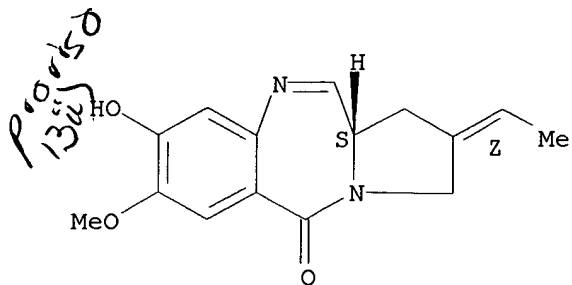
AB Antibacterial and anticarcinogenic (no data) benzodiazepine derivs. I and II ( $R = R_3 = H$ ,  $R_1 = Me$ ,  $R_2 = HO$ ;  $R = R_3 = HO$ ,  $R_1 = R_2 = H$ ) were prepd. by reductive cyclization of III [ $R_4-R_7 = H$ ,  $MeO$ , (protected)  $HO$ ;  $R_8 = CHO$ ]. Thus, reaction of N-(tert-butoxycarbonyl)-4-oxo-L-proline  $Ph_2CH$  ester with  $EtPh_3PBr$  followed by deprotection gave (4Z)-ethylidene-L-proline  $Ph_2CH$  ester, whose acylation with IV in  $EtOAc$  contg.  $Et_3H$  at room temp. gave III ( $R_4 = R_7 = H$ ,  $R_5 = MeO$ ,  $R_6 = PhCH_2O$ ,  $R_8 = CO_2CHPh_2$ ), treatment of which with  $F_3CCO_2H$  in  $PhOMe$  at room temp. gave the corresponding III ( $R_8 = CO_2H$ ), whose hydride redn. gave III ( $R_8 = CHO$ ), hydrogenation of which over  $Pd/BaSO_3$  at room temp. for 3 h gave (2Z,11aS)-I.

IT **81422-29-9P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 81422-29-9 CAPLUS

09/763,767

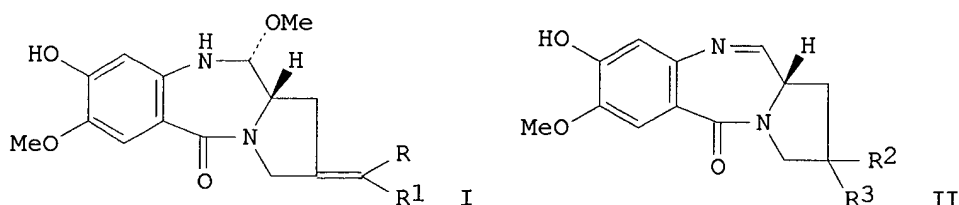
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



09/763,767

~~LA~~ 6 ANSWER 88 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1983:422186 CAPLUS  
DN 99:22186  
TI Studies on tomaymycin. II. Total syntheses of the antitumor antibiotics,  
E- and Z-tomaymycins  
AU Tozuka, Zenzaburo; Takasugi, Hisashi; Takaya, Takao  
CS Res. Lab., Fujisawa Pharm. Co., Ltd., Osaka, Japan  
SO J. Antibiot. (1983), 36(3), 276-82  
CODEN: JANTAJ; ISSN: 0021-8820  
DT Journal  
LA English  
GI

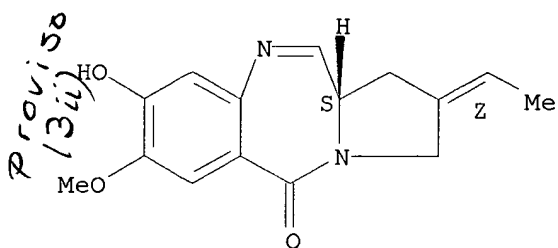


AB Naturally occurring E-tomaymycin (I, R = Me, R1 = H) and its Z-isomer (I, R = H, R1 = Me) were prepd. from hydroxyproline. Unsatd. analogs II (R2 = OH, R3 = H; R2R3 = CHMe) were also prepd. Z-I had the same antibacterial activity as E-I.

IT **81422-29-9P 81422-30-2P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and methanolysis of)

RN 81422-29-9 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

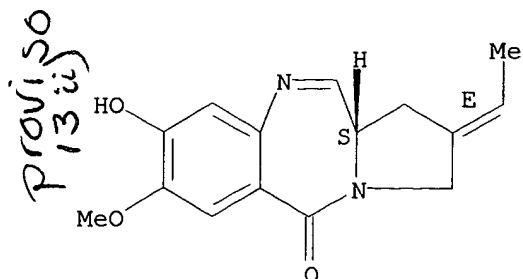


RN 81422-30-2 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



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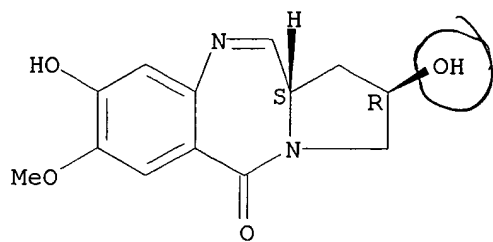
IT **85993-77-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 85993-77-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy-, (2R-cis)- (9CI) (CA INDEX NAME)

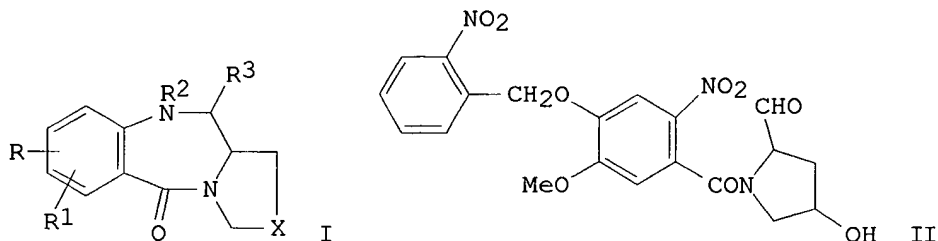
Absolute stereochemistry.



09/763,767

~~126~~ ANSWER 89 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1983:72145 CAPLUS  
DN 98:72145  
TI Benzodiazepine derivatives  
PA Fujisawa Pharmaceutical Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 12 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 57131791	A2	19820814	JP 1981-216205	19811228
	JP 02016315	B4	19900416		
PRAI	GB 1980-41626		19801231		
GI					



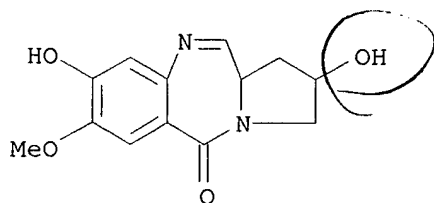
AB Title compds. I (R = OH; R1 = alkoxy; R2 = H; R3 = alkoxy; R2R3 = bond; X = CHO, S, CO, C:CHCN, C:NR5, R5 = alkoxy), useful as bactericides, and antineoplastics (data given), were prepd. Thus, reductive cyclization of pyrrolidine II with 10% Pd/C gave I (R = 8-OH, R1 = 7-MeO, R2R3 = bond, X = CHO).

IT **81306-70-9P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. and antineoplastic activity of)

RN 81306-70-9 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy- (9CI) (CA INDEX NAME)



IT **84447-45-0P 84447-47-2P 84447-48-3P**

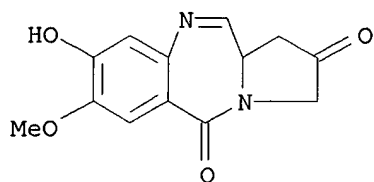
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 84447-45-0 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione,

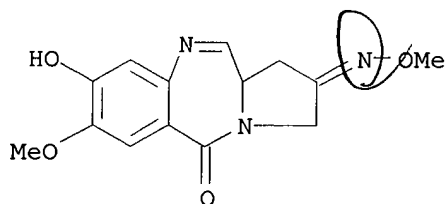
09/763,767

8-hydroxy-7-methoxy- (9CI) (CA INDEX NAME)



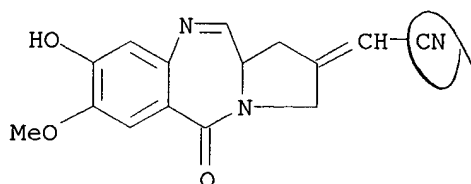
RN 84447-47-2 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione,  
8-hydroxy-7-methoxy-, 2-(O-methyloxime) (9CI) (CA INDEX NAME)



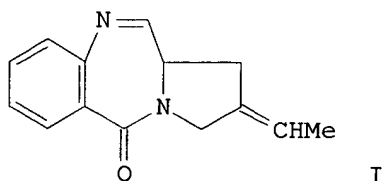
RN 84447-48-3 CAPLUS

CN Acetonitrile, (5,11a-dihydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene)- (9CI) (CA INDEX NAME)



09/763,767

~~126~~ ANSWER 90 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1982:578414 CAPLUS  
DN 97:178414  
TI Prothracarcin, a novel antitumor antibiotic  
AU Shimizu, Kenichi; Kawamoto, Isao; Tomita, Fusao; Morimoto, Makoto;  
Fujimoto, Kazuhisa  
CS Tokyo Res. Lab., Kyowa Hakko Kogyo Co. Ltd., Tokyo, Japan  
SO J. Antibiot. (1982), 35(8), 972-8  
CODEN: JANTAJ; ISSN: 0021-8820  
DT Journal  
LA English  
GI



AB A novel antibiotic, prothracarcin (I), was isolated from the culture broth of *Streptomyces umbrosus raffinophilus* DO-62. The antibiotic has the mol. formula  $C_{14}H_{14}N_2O$  and belongs to the pyrrolo[1,4]benzodiazepine antibiotics. Its structure was elucidated by mass and NMR spectra. It is active against gram-pos. and gram-neg. bacteria and exptl. murine tumor sarcoma 180 and leukemia P388.

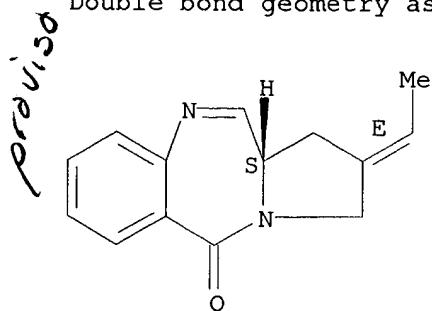
IT **81542-99-6**

RL: BIOL (Biological study)  
(antibiotic, from *Streptomyces umbrosus*)

RN 81542-99-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (2E,11aS)- (9CI) (CA INDEX NAME)

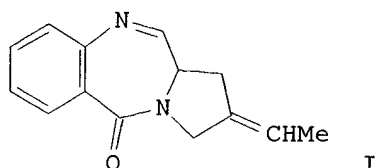
Absolute stereochemistry.  
Double bond geometry as shown.



09/763,767

L26 ANSWER 91 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1982:179428 CAPLUS  
DN 96:179428  
TI Antibacterial and anticarcinogenic DC-62  
PA Kyowa Hakko Kogyo Co., Ltd., Japan  
SO Jpn. Kokai Tokkyo Koho, 6 pp.  
CODEN: JKXXAF  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 56158785	A2	19811207	JP 1980-62256	19800513
	JP 63030916	B4	19880621		
GI					



AB Antibacterial and anticarcinogenic DC-62 (I) was prepd. by cultivation of *Streptomyces umbrosus raffinophilus* DC-62 and isolated from the culture broth. Min. inhibitory concns. of I were 50, 50, 50, >100, and >100 .mu.g/mL against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Sarcina typhosa*, and *Shigella sonnei*, resp. Anticarcinogenic activity of I was demonstrated against Sarcoma 180 solid tumor and lymphocytic leukemia P-388 tumor cells, in mice; LD50 of I was 42 mg/kg i.p. in mice. Thus, precultured *S. umbrosus raffinophilus* (Bikoken 5468, NRRL 12143) was cultured on 15 L broth (pH 7) comprising molasses 10 (as glucose), corn steep liquor 10, NaCl 1, KCl 10, MnSO4.cntdot.H2O 2, NH4H2PO4 1, and L-lysine 40 g/L for 72 h at 30.degree. under 15 L/min aeration. I was chromatographed over Diaion HP-10 and Sephadex LH-20 to yield 10 mg I. The IR spectra of I are presented.

IT 81542-99-6

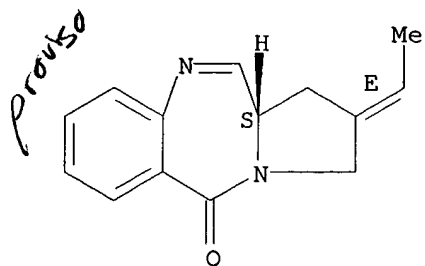
RL: BIOL (Biological study)  
(from *Streptomyces umbrosus*, as tumor inhibitor)

RN 81542-99-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

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09/763,767

see  
89 9/107

L26 ANSWER 92 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1982:162399 CAPLUS  
DN 96:162399  
TI Syntheses of tomaymycin and its analogs  
AU Tozuka, Zenzaburo; Takaya, Takao  
CS Res. Lab., Fujisawa Pharm. Co. Ltd., Japan  
SO Tennen Yuki Kagobutsu Toronkai Koen Yoshishu, 24th (1981), 552-9  
Publisher: Osaka Univ., Fac. Pharm. Sci., Suita, Japan.  
CODEN: 47BNAB  
DT Conference  
LA Japanese  
GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Tomaymycin [(E)-I] and (Z)-I were prep'd. from L-hydroxyproline (II) and vanillin (III) in several steps. Proline IV was acylated with acid chloride V to give benzoylproline VI (R = OCHPh<sub>2</sub>), which was converted to VI (R = H), which was converted to (E)- and (Z)-I or to dehydro derivs. (E)- and (Z)-VII. IV and V were prep'd. from II and III, resp. The structure and configuration of (E)-I were det'd. by H and <sup>13</sup>C NMR data. Several tomaymycin analogs were also prep'd.

IT **81422-29-9P 81422-30-2P**

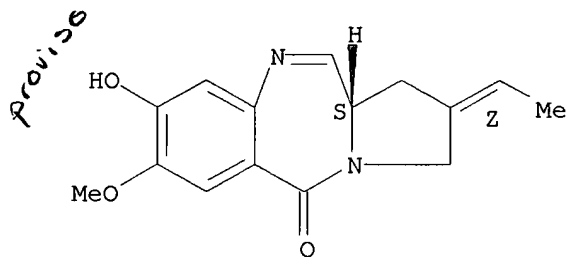
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and NMR of)

RN 81422-29-9 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, [S-(Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.



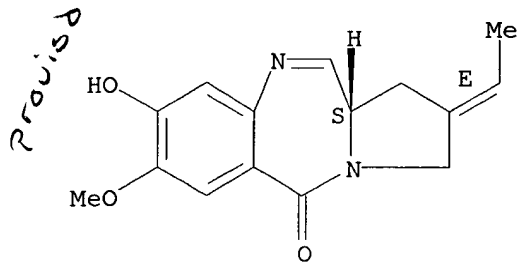
RN 81422-30-2 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 2-ethylidene-1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (2E,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

09/763,767

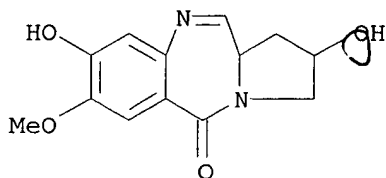


IT 81306-70-9P 81306-73-2P 81306-74-3P  
81306-75-4P 81306-76-5P 81306-77-6P  
81307-24-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 81306-70-9 CAPLUS

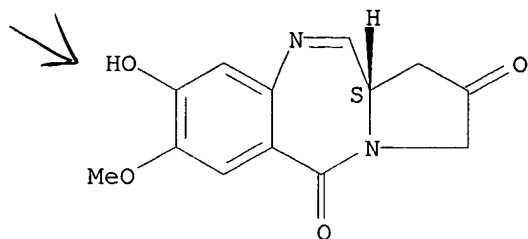
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-2,8-dihydroxy-7-methoxy- (9CI) (CA INDEX NAME)



RN 81306-73-2 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione, 8-hydroxy-7-methoxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 81306-74-3 CAPLUS

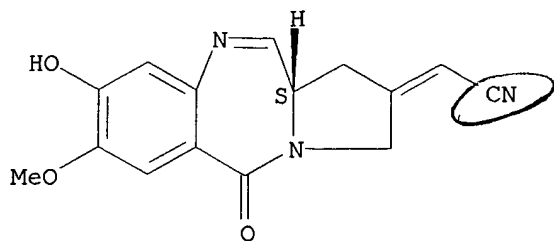
CN Acetonitrile, (5,11a-dihydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2(3H)-ylidene)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.



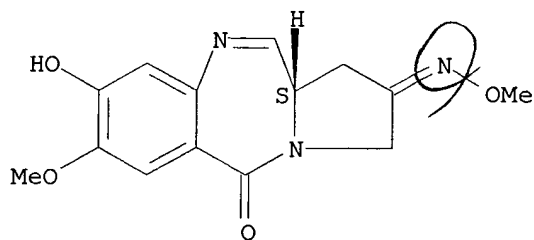
09/763,767



RN 81306-75-4 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione,  
8-hydroxy-7-methoxy-, 2-(O-methyloxime), (S)- (9CI) (CA INDEX NAME)

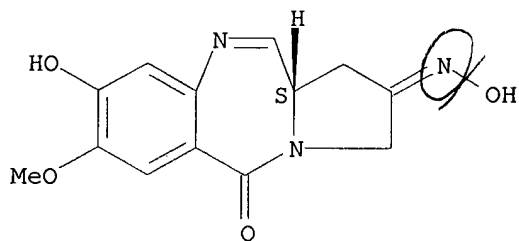
Absolute stereochemistry.  
Double bond geometry unknown.



RN 81306-76-5 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2,5(3H,11aH)-dione,  
8-hydroxy-7-methoxy-, 2-oxime, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry unknown.

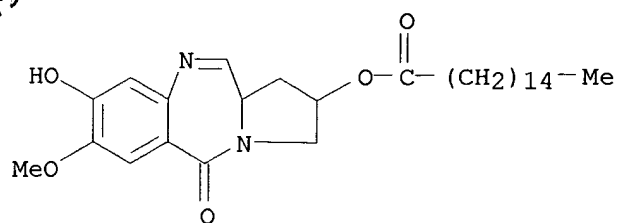


RN 81306-77-6 CAPLUS

CN Hexadecanoic acid, 2,3,5,11a-tetrahydro-8-hydroxy-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl ester (9CI) (CA INDEX NAME)

09/763,767

Provisio

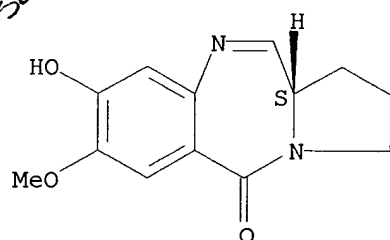


RN 81307-24-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-8-hydroxy-7-methoxy-, (11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

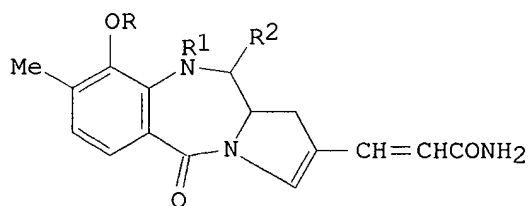
Provisio



09/763,767

~~125~~ ANSWER 93 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1981:139855 CAPLUS  
 DN 94:139855  
 TI Benzodiazepines  
 PA Green Cross Corp., Japan  
 SO Belg., 24 pp.  
 CODEN: BEXXAL  
 DT Patent  
 LA French  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 882305	A1	19800716	BE 1980-199851	19800319
	JP 56015289	A2	19810214	JP 1979-89886	19790717
	JP 62037631	B4	19870813		
	SE 8001458	A	19810118	SE 1980-1458	19800225
	SE 436882	B	19850128		
	SE 436882	C	19850509		
	CA 1152985	A1	19830830	CA 1980-346511	19800227
	US 4309437	A	19820105	US 1980-127984	19800304
	GB 2053894	A	19810211	GB 1980-8033	19800310
	GB 2053894	B2	19830420		
	NL 8001531	A	19810120	NL 1980-1531	19800314
	DE 3010544	A1	19810129	DE 1980-3010544	19800319
	DE 3010544	C2	19820701		
	FR 2461711	A1	19810206	FR 1980-6153	19800319
	FR 2461711	B1	19830513		
	CH 648848	A	19850415	CH 1980-2187	19800320
PRAI	JP 1979-89886		19790717		
GI					



AB Pyrrolobenzodiazepines I (R = H, acyl, CONH2, alkoxycarbonyl; R1 = H, acyl; R2 = SO2H) were prepd. by treating I (R2 = OMe) with Na dithionite. I (R2 = SO3H) were prepd. by oxidizing I (R2 = SO2H) or by treating I (R2 = OMe) with SO2 or K2SO3. Thus, 1 g I (R = R1 = Ac, R2 = OMe) was treated with Na dithionite to give 0.8 g I (R = R1 = Ac, R2 = SO2H), which at 0.12 mg/kg daily i.p. for 6 days increased the survival time of leukemia P388 infected mice by 190%.

IT **14435-72-4**

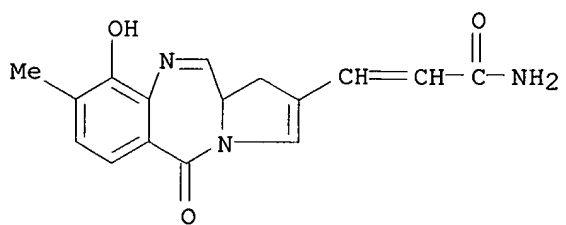
RL: RCT (Reactant)  
 (sulfonation of)

RN 14435-72-4 CAPLUS

CN 2-Propenamide, 3-(5,10,11,11a-tetrahydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)- (9CI) (CA INDEX NAME)

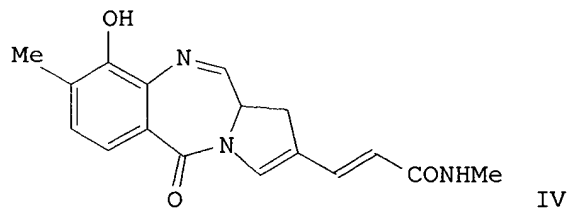
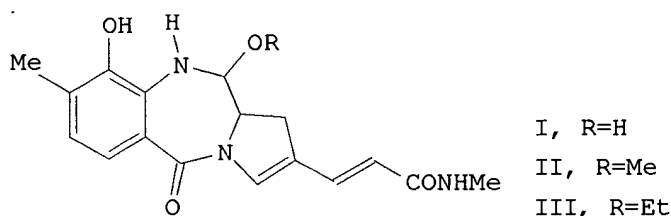
09/763,767

Provi 500



09/763,767

126 ANSWER 94 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1980:636828 CAPLUS  
DN 93:236828  
TI Mazethramycin, a new member of anthramycin group antibiotics  
AU Kunitomo, Setsuko; Masuda, Toru; Kanbayashi, Nobuo; Hamada, Masa;  
Naganawa, Hiroshi; Miyamoto, Masashi; Takeuchi, Tomio; Umezawa, Hamao  
CS Inst. Microbial Chem., Tokyo, 141, Japan  
SO J. Antibiot. (1980), 33(6), 665-7  
CODEN: JANTAJ; ISSN: 0021-8820  
DT Journal  
LA English  
GI



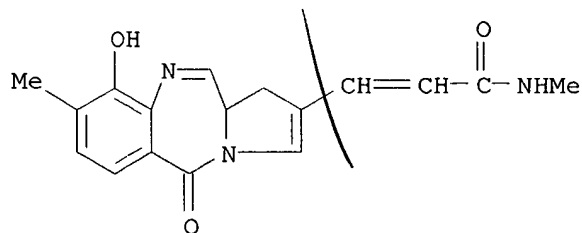
AB Mazethramycin (I) [68373-96-6] was produced by fermn. with *Streptomyces thioluteus*. The Me ether (II) [68373-95-5], Et ether (III) [68373-94-4], and anhydro (IV) [68373-93-3] derivs. were obtained by chem. treatment. II inhibited gram-pos. and gram-neg. bacteria and prolonged the survival of mice infected with leukemia L-1210 cells.

IT **68373-93-3P**

RL: PREP (Preparation)  
(prepn. of)

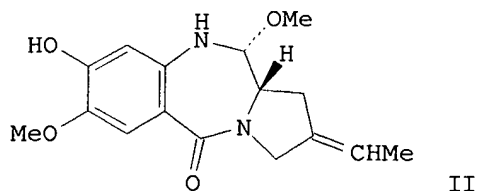
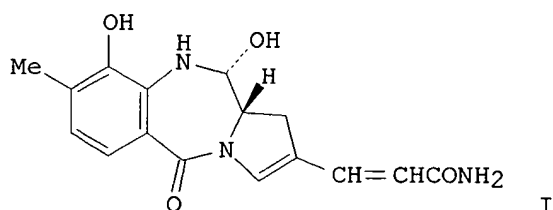
RN 68373-93-3 CAPLUS

CN 2-Propenamide, 3-(5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)-N-methyl- (9CI) (CA INDEX NAME)



09/763,767

~~126~~ ANSWER 95 OF 107 CAPLUS. COPYRIGHT 2001 ACS  
AN 1980:51709 CAPLUS  
DN 92:51709  
TI Antitumor antibiotics. XVI. Molecular mechanism of binding of  
pyrrolo(1,4)benzodiazepine antitumor agents to deoxyribonucleic acid.  
Anthramycin and tomaymycin  
AU Lown, J. William; Joshua, Alummoottil V.  
CS Dep. Chem., Univ. Alberta, Edmonton, AB, T6G 2G2, Can.  
SO Biochem. Pharmacol. (1979), 28(13), 2017-26  
CODEN: BCPA6; ISSN: 0006-2952  
DT Journal  
LA English  
GI



AB The extent of binding of the pyrrolo[1,4]benzodiazepine antibiotics, anthramycin (I) [4803-27-4] and tomaymycin (II) [35050-55-6], to DNA, measured by suppression of ethidium fluorescence, was proportional to the antibiotic concn. and was partly reversed by a heat-denaturation-renaturation cycle. The extent of binding of I and II to DNA was promoted by lower pH (4.7-9) and higher temps. (0-51.degree.), and the DNA-antibiotic complex was stable to dialysis. There was no evidence that these antibiotics intercalate into DNA, but they were more reactive toward relaxed PM2-DNA than to supercoiled DNA. Examn. of DNA binding of the antibiotics and their analogs to DNAs of different base compn. and sep. in conjugation with sequence specific binding agents showed little base preference for binding. Reaction of the antibiotics with DNA produced neither depurination nor strand scission. A free or potential carbinolamine or imine function at the 10,11 positions in a benzo[1,4]diazepine nucleus was an abs. requirement for DNA binding or of reaction with nucleophiles.

IT **72435-89-3P**

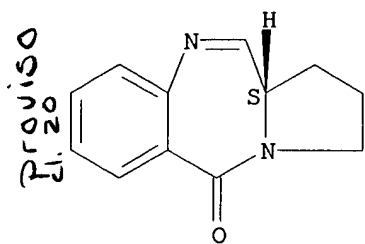
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of and DNA binding to, antitumor activity in relation to)

RN 72435-89-3 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-, (11aS)-  
(9CI) (CA INDEX NAME)

09/763,767

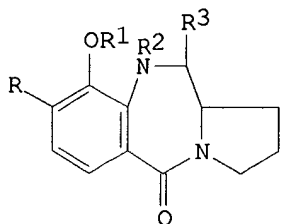
Absolute stereochemistry. Rotation (+).



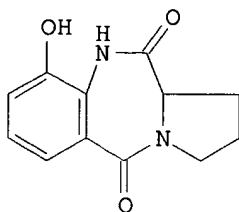
09/763,767

~~126~~ ANSWER 96 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1979:540872 CAPLUS  
DN 91:140872  
TI Pyrrolobenzodiazepines useful in treating tumors  
IN Takanabe, Atsuyuki; Arakawa, Yoshio; Kagitani, Yoshio; Ueda, Yasuo; Satoh, Daisuke; Komatsu, Nobuhiko  
PA Green Cross Corp., Japan  
SO Ger. Offen., 45 pp.  
CODEN: GWXXBX  
DT Patent  
LA German  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	DE 2844292	A1	19790628	DE 1978-2844292	19781011
	JP 54090195	A2	19790717	JP 1977-156684	19771227
	JP 58005916	B4	19830202		
	US 4185016	A	19800122	US 1978-947418	19781002
	US 4239683	A	19801216	US 1979-42449	19790525
PRAI	JP 1977-156684		19771227		
	US 1977-947418		19771002		
GI					



I



II

AB The pyrrolobenzodiazepines I (R = H, OH, alkyl, alkoxy; R1 = H, acyl; R2R3 = bond; R2 = H, R3 = OR4; R4 = H, alkyl, phenylalkyl) were prepd. and tested for antitumor activity (test data tabulated). Thus, L-proline Me ester reacted with 3,2-(HO)(O2N)C6H3CO2H, and the product was hydrogenated, followed by refluxing in xylene to give II. This was treated with PhCH(OMe)2, followed by reaction with NaBH4 in MeOH to give I (R-R2 = H, R3 = OMe), which at 5 mg/kg prolonged the life of mice infected with Leukemia P388 by 148.0%.

IT **71444-82-1P 71444-83-2P 71444-84-3P**

**71444-90-1P 71445-00-6P 71445-01-7P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. and antitumor activity of)

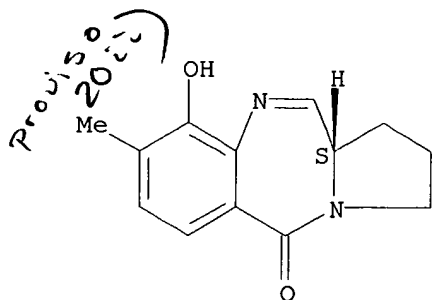
RN 71444-82-1 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-8-methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

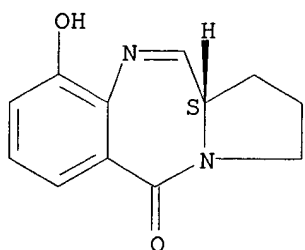


09/763,767



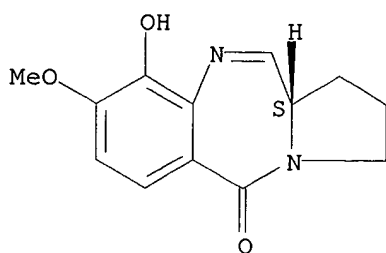
RN 71444-83-2 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 71444-84-3 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 1,2,3,11a-tetrahydro-9-hydroxy-8-methoxy-, (S)- (9CI) (CA INDEX NAME)

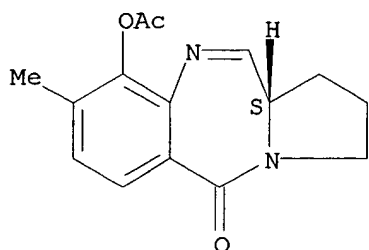
Absolute stereochemistry.



RN 71444-90-1 CAPLUS  
CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-(acetyloxy)-1,2,3,11a-tetrahydro-8-methyl-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

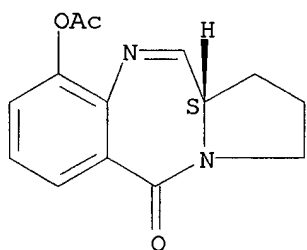
09/763,767



RN 71445-00-6 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-(acetyloxy)-1,2,3,11a-tetrahydro-, (S)- (9CI) (CA INDEX NAME)

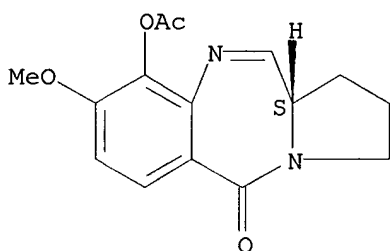
Absolute stereochemistry.



RN 71445-01-7 CAPLUS

CN 5H-Pyrrolo[2,1-c][1,4]benzodiazepin-5-one, 9-(acetyloxy)-1,2,3,11a-tetrahydro-8-methoxy-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



09/763,767

~~126~~ ANSWER 97 OF 107 CAPLUS COPYRIGHT 2001 ACS

~~7N~~ 1979:4427 CAPLUS

DN 90:4427

TI Mazethramycins

IN Umezawa, Hamao; Takeuchi, Tomio; Hamada, Masashi; Kunimoto, Setsuko

PA Microbiochemical Research Foundation, Japan

SO Jpn. Kokai Tokkyo Koho, 24 pp.

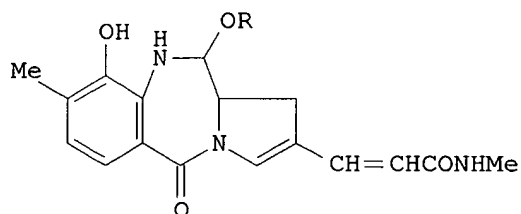
CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

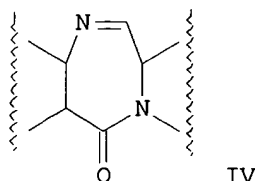
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 53082792	A2	19780721	JP 1976-157479	19761228
	JP 60053033	B4	19851122		
GI					



I, R=H

II, R=Me

III, R=Et



AB Mazethramycin A (I) [68373-96-6], mazethramycin B (II) [68373-95-5], mazethramycin C (III) [68373-94-4], and anhydromazethramycin (IV) [68373-93-3] were prepd. by cultivation of *Streptomyces thioluteus* ME 561-14 followed by chem. treatment. I-IV had antibacterial and antileukemic activities. Thus, *S. thioluteus* ME 561-14 was precultured on a liq. broth of glycine 1.5, cottonseed meal 1.5, L-asparagine 0.2, and NaCl 0.3% for 48 h at 27.degree. and then cultured for 4 days at 27.degree. to give 216 mg I-IV in the culture. The culture was made pH 8.0, extd. with BuOH, dissolved in H<sub>2</sub>O, and chromatographed on Amberlite XAD and SiO<sub>2</sub> gel to give 71 mg II. Refluxing 124 mg II with Amberlite CG-80 in MeCN for 1 h gave 80 mg IV, which was dissolved in 50% aq. Me<sub>2</sub>CO and concd. to give I, which (50 mg) was dissolved in EtOH and concd. to give 45 mg III. IR and UV spectra of I-III and the NMR spectrum of II are given.

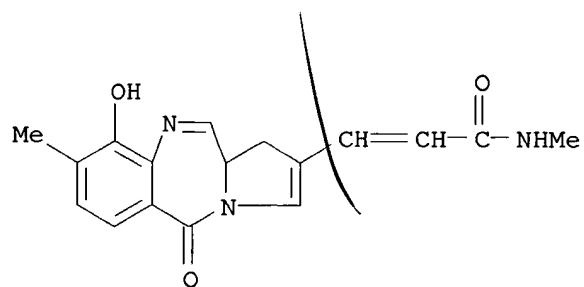
IT 68373-93-3

RL: BIOL (Biological study)  
(antibiotic, from *Streptomyces thioluteus*)

RN 68373-93-3 CAPLUS

CN 2-Propenamide, 3-(5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)-N-methyl- (9CI) (CA INDEX NAME)

09/763,767



~~D26~~ ANSWER 98 OF 107 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1975:477004 CAPLUS

~~DN~~ 83:77004

~~TI~~ Chemotherapeutic benzodiazepine derivatives by cultivating pretomeimycin-producing Streptomyces strain, treating with lower alcohol then nonalcoholic solvent

~~IN~~ Arima, Hiroshi; Tamura, Takazo; Sakai, Heiichi; Mukosaka, Masanobu

~~PA~~ Fujisawa Pharmaceutical Co., Ltd., Japan

~~SO~~ Japan., 14 pp. Division of Japan. Koho 73 00,076 (See Ger. 1,965,304, CA 73:77291k).

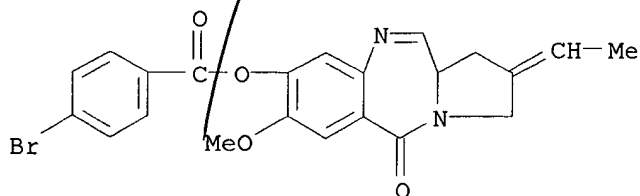
CODEN: JAXXAD

~~DT~~ Patent

~~LA~~ Japanese

~~FAN.CNT~~ 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 49025957	B4	19740704	JP 1970-99200	19701110
GI	For diagram(s), see printed CA Issue.				
AB	Benzodiazepines (I; R = lower alkyl; R1 = halobenzoyl or H) were prepd. from pretomeimycin isolated from (or without isolation) cultures of Streptomyces by treating with lower alcs. Thus, S. achromogenes tomaymyceticus was cultured aerobically at 30.degree. for 50-60 hr in a medium contg. lactose 3, meat ext. 1, yeast 1, polypeptone 1, NaCl 0.25, KH2PO4 1.5, and Na2HPO4 0.43%. The culture was centrifuged and the supernatant was worked up to yield pretomeimycin. Pretomeimycin was dissolved in EtOAc, adsorbed on a silicate column, and eluted with EtOAc. The eluate was evapd. to near dryness. The residue was dissolved in MeOH. The soln. was allowed to stand at -20.degree. for 2 days. Ppt. formed was 2,3,5,10,11,11a-hexahydro-2-ethylidene-7,11-dimethoxy-8-hydroxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepine (I; R = Me; R1 = H).				
IT	<b>28797-41-3</b>				
	RL: PROC (Process)				
	(fermn. of, benzodiazepine derivs. from)				
RN	28797-41-3 CAPLUS				
IT	<b>28797-41-3P 28797-43-5P</b>				
	RL: PREP (Preparation)				
	(prepn. of)				
RN	28797-41-3 CAPLUS				
RN	28797-43-5 CAPLUS				
CN	Benzoic acid, 4-bromo-, 2-ethylidene-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-8-yl ester (9CI) (CA INDEX NAME)				



See 98 of 107

09/763,767

126 ANSWER 99 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1975:458899 CAPLUS

DN 83:58899

TI Antibiotic pretomeimycin lower alcohol adducts having anti-microbial, anti-phage, and anti-viral activity

IN Arima, Hiroshi; Tamura, Takazo; Sakai, Heichi; Mukosaka, Masanobu

PA Fujisawa Pharmaceutical Co., Ltd., Japan

SO Japan., 12 pp. Division of Japan. Koho 73 00,076 (See Ger. 1,965,304, CA 73:77291k).

CODEN: JAXXAD

DT Patent

LA Japanese

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 49025956	B4	19740704	JP 1970-99199	19701110

GI For diagram(s), see printed CA Issue.

AB Pyrrolobenzodiazepines (I, R = lower alkyl) were prepd. by treating pretomeimycin with a lower alc. or cultivating a pretomeimycin-producing Streptomyces and treating the culture medium with a lower alc. Thus, 20 g pretomeimycin in EtOAc was treated with .apprx.30 ml MeOH at -20.degree. for 2 days to give 18 g I (R = Et).

IT **28797-41-3**

RL: RCT (Reactant)

(reaction with alcs.)

RN 28797-41-3 CAPLUS

proviso  
13 ii)

09/763,767

~~D26~~ ANSWER 100 OF 107 CAPLUS COPYRIGHT 2001 ACS  
~~AN~~ 1975:140209 CAPLUS  
DN 82:140209  
TI 8-Alkoxyalted benzodiazepine derivatives  
IN Arima, Hiroshi; Tamura, Takazo; Sakai, Heiichi; Mukosaka, Masanobu  
PA Fujisawa Pharmaceutical Co., Ltd.  
SO Japan., 2 pp. Division of Japan. 73 76 (See Ger. 1,965,304, CA 73:  
77291k).  
CODEN: JAXXAD  
DT Patent  
LA Japanese  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	JP 49025958	B4	19740704	JP 1970-99201	19701110
GI	For diagram(s), see printed CA Issue.				
AB	The bactericidal and virucidal (no data) pyrrolobenzodiazepine I (R = R1 = Me) was prepd. by treating pretomeimycin with MeOH and methylating I (R = Me, R1 = H) with CH2N2.				
IT	<b>55128-21-7</b>				
	RL: RCT (Reactant)				
	(reaction of, with methanol)				
RN	55128-21-7 CAPLUS				

*proviso  
(3 ii)*

09/763,767

~~L26~~ ANSWER 101 OF 107 CAPLUS COPYRIGHT 2001 ACS

~~AN~~ 1972:57720 CAPLUS

DN 76:57720

TI Antibiotic production utilizing *Streptomyces refuineus* var *thermotolerans*

IN Berger, Julius; Karr, Andrew E.; Leimgruber, Willy; Tabenkin, Benjamin;  
Schocher, Arno J.; Stefanovic, Vladimir

PA Hoffmann-La Roche Inc.

SO U.S., 9 pp. Division of U.S. 3,361,742 (CA 68:58569n).

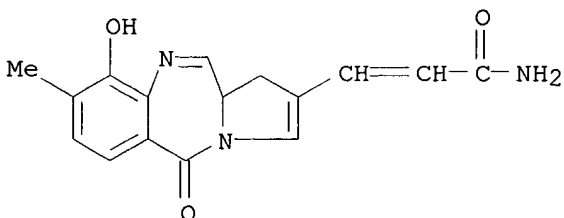
CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3619374	A	19711109	US 1967-687433	19671204
AB	The title bacterium (NRRL 3143 and 3144) was grown under agitated, aerobic fermentation conditions in aq. nutrient media contg. sources of carbohydrate and protein at 35-55.degree. for 12-15 hr at pH 6-8.5 and thereafter at pH 6-6.9. The culture filtrate was extd. with a solvent having low miscibility with water, esp. butanol, to yield an antibiotic-contg. ext. having antitumor and antibacterial activity.				
IT	<b>14435-72-4</b> RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study) (antibiotic activity of)				
RN	14435-72-4 CAPLUS				
CN	2-Propenamamide, 3-(5,10,11,11a-tetrahydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)- (9CI) (CA INDEX NAME)				

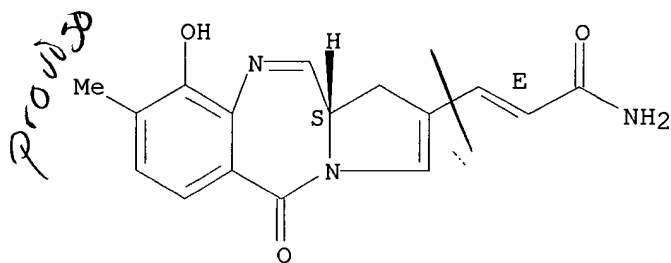




09/763,767

~~126~~ ANSWER 102 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1972:21926 CAPLUS  
DN 76:21926  
TI Chemosterilant action of anthramycin. Proposed mechanism  
AU Horwitz, Susan B.  
CS Dep. Pharmacol., Albert Einstein Coll. Med., New York, N. Y., USA  
SO Science (1971), 174(4005), 159-61  
CODEN: SCIEAS  
DT Journal  
LA English  
AB The activity of anthramycin (I) [4803-27-4] and structurally related  
analogs as chemosterilants of the housefly, *Musca domestica*, correlated  
closely with the action of these compds. as inhibitors of *Escherichia coli*  
RNA polymerase. Since inhibition of RNA polymerase by I reflects binding  
of this antibiotic to the DNA primer required for enzyme activity, the  
interaction of I with DNA may also account for its action as a  
chemosterilant.  
IT **16758-27-3**  
RL: BIOL (Biological study)  
(as chemosterilants)  
RN 16758-27-3 CAPLUS  
CN 2-Propenamide, 3-[(11aS)-5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-1H-  
pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



26 ANSWER 103 OF 107 CAPLUS COPYRIGHT 2001 ACS

AN 1970:531049 CAPLUS

DN 73:131049

TI Antiprotozoal, anthelmintic, and antitumor benzodiazepine compounds

IN Leimgruber, Willy; Schenker, Fausto E.

PA Hoffmann-La Roche Inc.

SO U.S., 13 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3523941	A	19700811	US 1967-620618	19670306

GI For diagram(s), see printed CA Issue.

AB The acetates of I and II were prepd. by acylation of the corresponding 9-OH deriv. I (R1 = R2 = H, R3 = .alpha.-OMe) (III), or its hydrate. The epimers of I were prepd. by acylating III, removing the elements of MeOH from the mol. by an 8 hr reflux with H2C:C(Me)OAc and treating the product with MeOH at room temp. Thus, III in 1:1 Ac2O-NEt3 stirred 4 hr at 20.degree. gave (11R,11aS)-5,10,11,11a-tetrahydro-9-hydroxy-11-methoxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepine-2-trans-acrylamide acetate (IV). (11S,11aS)-Epimer of IV was similarly prepd. and had the same activity against S 180 and Ehrlich solid tumors in mice. II (R1 = H) stirred 2 hr at 20.degree. in 1:1 Ac2O-C5H5N gave II (R1 = Ac) (V). V in 4:1 H2O-Me2CO kept 18 hr at 20.degree. gave I (R1 = H, R2 = Ac, R3 = OH) (VI). V in C5H5N kept 3 days at 20.degree. in AcOH-Ac2O gave I (R1 = R2 = Ac, R3 = AcO). Treatment of III.H2O with (EtCO)2O-NEt3, (PrCO)2O-NEt2, or Bz3O-NEt3 gave I (R1 = EtCO, PrCO, or Bz). Similar acylations of III.H2O with PhNCO, EtNCO, or (EtO)2CO in the presence of NEt3 gave I (R1 = PhNHCO, EtNHCO, EtCO2). I are useful as antitumor agents against Sarcoma 180 and Ehrlich solid tumors in mice, as antiprotozoal agents against Entamoeba histolytica and Trichomonas vaginalis, and as anthelmintic agents against Syphacia obvelata.

IT 29775-04-0P

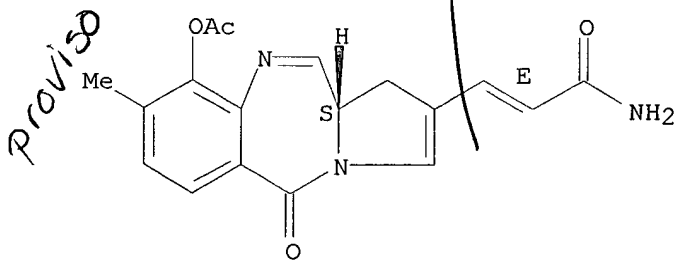
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 29775-04-0 CAPLUS

CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acrylamide, 5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-, acetate (ester), (E)-(S)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

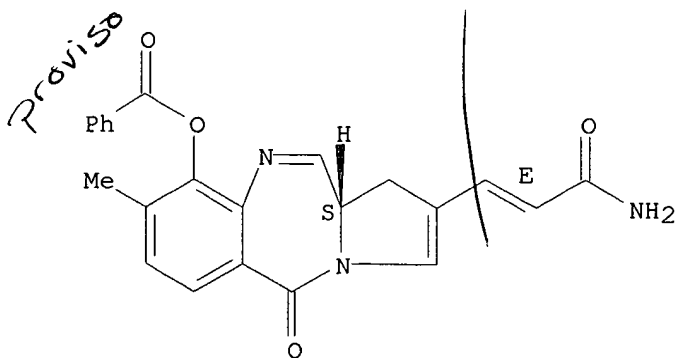


09/763,767

126 ANSWER 104 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1970:520692 CAPLUS  
DN 73:120692  
TI Antitumor pyrrolobenzodiazepine acrylamides and intermediates  
IN Batcho, Andrew D.; Leimgruber, Willy  
PA Hoffmann-La Roche Inc.  
SO U.S., 12 pp.  
CODEN: USXXAM  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3524849	A	19700818	US 1967-678532	19671027
GI	For diagram(s), see printed CA Issue.				
AB	The title antitumor agents I (R = H or Me) were prepd. from 3-benzyloxy-2-nitro-p-toluoyl chloride (II) and L-(4-hydroxyproline) Me ester (III). Thus, II was treated at 20-25.degree. with III in CH <sub>2</sub> Cl <sub>2</sub> contg. Et <sub>3</sub> N to give 1-(3-benzyloxy-2-nitro-p-toluoyl)-L-(4-hydroxyproline) Me ester which was treated with aq. Na <sub>2</sub> S <sub>2</sub> O <sub>6</sub> in THF at 40.degree. to give 1-(3-benzyloxy-2-amino-p-toluoyl)-L-(4-hydroxyproline) Me ester (IV). A xylene soln. of IV was refluxed overnight to give (2R,-11aS)-9-benzyloxy-1,2,3, 11a-tetrahydro-2-hydroxy-8-methyl-5H-pyrrolo[2,1-c][1,4]benzodiazepine-5, 11(10H)-dione, m. 243-3.5.degree. (vac.), which was oxidized to (11aS)-9-benzyloxy-8-methyl-1H-pyrrolo[2,1-c][1,4]benzodiazepine-2,5, 11(3H,10H,11aH)-trione (VI). Treatment of VI with Et <sub>3</sub> PCH <sub>2</sub> CO <sub>2</sub> Et gave VII (R = CO <sub>2</sub> Et). This was converted to VII (R = CHO), VII [R = CH(OH)CN], and VII [R = CH(O <sub>3</sub> Me)CN], which gave VIII when treated with base. The reaction between VIII and F <sub>3</sub> C-CO <sub>2</sub> H gave the 9-OH analog of VIII which was treated with PhCH(OMe) <sub>2</sub> to give IX (R = CN). IX (R = CN) was hydrolyzed in polyphosphoric acid to IX (R = CONH <sub>2</sub> ) which was reduced with LiAlH <sub>4</sub> -THF at -50.degree. to X. Treatment of X with MeOH-HCl gave I (R = Me).				
IT	<b>29169-51-5P 29217-57-0P</b> RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)				
RN	29169-51-5 CAPLUS				
CN	1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acrylamide, 5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-, benzoate (ester), (E)-(S)-(+)-(8CI) (CA INDEX NAME)				

Absolute stereochemistry.  
Double bond geometry as shown.



RN 29217-57-0 CAPLUS

~~126~~ ANSWER 105 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1970:477291 CAPLUS  
 DN 73:77291

TI Microbicial and antitumorous 2-ethylidene-7-methoxy-8-hydroxy-  
 1,2,3,10,11,11a-hexahydro-5H-pyrrolo [2,1-c] [1,4]benzodiazepin-5-ones  
 from a new Streptomyces

IN Arima, Kei; Tamura, Gakuzo; Sakai, Heiichi; Kosaka, Masanobu; Yazawa,  
 Hisatoyo; Kariyone, Kazuo

PA Fujisawa Pharmaceutical Co., Ltd.

SO Ger. Offen., 39 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 1965304	A	19700723	DE 1969-1965304	19691229
	JP 48000076	A2	00000000	JP 1969-83	19681230
	JP 48043755	B4	19731220	JP 1969-50780	19690626
	IL 33558	A1	19731025	IL 1969-33558	19691217
	ZA 6908792	A	19710331	ZA 1969-8792	19691218
	FI 46259	B	19721031	FI 1969-3710	19691222
	GB 1299198	A	19721206	GB 1969-1299198	19691224
	FR 2027356	A5	19700925	FR 1969-45316	19691229
	FR 2027356	B1	19740111		
	SU 474148	D	19750614	SU 1969-1877791	19691229
	CH 531564	A	19730131	CH 1969-531564	19691230
	CH 539062	A	19730831	CH 1972-7606	19691230
	CA 955595	A1	19741001	CA 1970-86357	19700623
	US 3794644	A	19740226	US 1970-49974	19700625
PRAI	JP 1969-83		19681230		
	JP 1969-50780		19690626		
	JP 1968-83		19681230		

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) with antiviral and antibacteriophagic activity were  
 prepd. by microbiol. formation of the powdery fundamental substance by  
 means of the new *S. achromogenes* var *tomaymyceticus* ATCC 21353 and  
 subsequent chem. reactions. Thus, the supernatant of a culture medium of  
 ATCC 21353 was extd. to give a powder, which gave with MeOH at -20.degree.  
 I (R = OMe, R1 = H) (Ia). Similarly prepd. was I (R = OEt, R1 = H).  
 Heating Ia in CHCl3 or AcOEt gave II (R1 = H) (IIa), which added MeOH to  
 regenerate Ia. Ia and CH2N2, Ac2O-pyridine, or (p-BrC6H4CO)2O-pyridine  
 gave I (R = OMe, R1 = Me), I (R = OMe, R1 = Ac), or crude I (R = OMe, R1 =  
 p-BrC6H4CO), resp. Treating the latter with MeCN gave II (R1 =  
 p-BrC6H4CO. IIa and PhCH2SH, EtSH, or Me2NH gave I (R = PhCH2S, R1 = H), I  
 (R = EtS, R1 = H), or I (R = Me2N, R1 = H). The uv and ir spectra of Ia  
 and its activity against several microorganisms were reported.

IT **28797-41-3P 28797-43-5P**

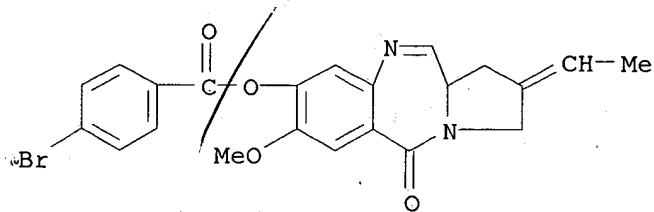
RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 28797-41-3 CAPLUS

RN 28797-43-5 CAPLUS

CN Benzoic acid, 4-bromo-, 2-ethylidene-2,3,5,11a-tetrahydro-7-methoxy-5-oxo-  
 1H-pyrrolo[2,1-c] [1,4]benzodiazepin-8-yl ester (9CI) (CA INDEX NAME)

09/763,767

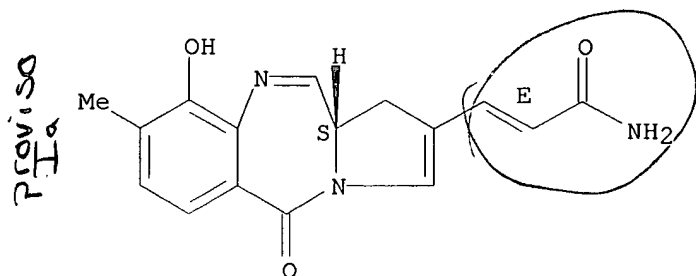


See 102-9107

09/763,767

~~LA~~ 6 ANSWER 106 OF 107 CAPLUS COPYRIGHT 2001 ACS  
AN 1968:85851 CAPLUS  
DN 68:85851  
TI Spectrophotometric studies of the interaction of anthramycin with deoxyribonucleic acid  
AU Stefanovic, Vladimir  
CS Hoffmann-LaRoche., Inc., Nutley, N. J., USA  
SO Biochem. Pharmacol. (1968), 17(2), 315-23  
CODEN: BCPCA6  
DT Journal  
LA English  
AB Qual. and quant. aspects of the interaction between anthramycin Me ether (I) and DNA were investigated spectrophotometrically by utilizing alterations in the I spectrum that result from complex formation. Certain nucleic acid polymers, purine and pyrimidine derivs., and various agents were employed in examg. the mol. nature of the interaction. These expts. suggest that binding involves both electrostatic attraction between I and the anionic phosphate groups of DNA, and a more specific interaction apparently involving 7-membered ring portions of I and DNA. The secondary structure of DNA also affects its binding to I. The ability of the compds. of the anthramycin series to complex with DNA was correlated with their biol. activity. The possibility of predicting biol. activity of a new compd. from this series by using only spectrophotometric assay is therefore indicated.  
IT **16758-27-3**  
RL: BIOL (Biological study)  
(complexing of, with deoxyribonucleic acid, antibiotic activity in relation to)  
RN 16758-27-3 CAPLUS  
CN 2-Propenamamide, 3-[(11aS)-5,11a-dihydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]-, (2E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.



see 101 of 101

09/763,767

~~E26~~ ANSWER 107 OF 107 CAPLUS COPYRIGHT 2001 ACS  
 AN 1968:58569 CAPLUS  
 DN 68:58569  
 TI 5-Oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2- acrylamides  
 IN Berger, Julius; Karr, Andrew E.; Leimgruber, Willy; Schocher, Arno J.;  
 Stefanovic, Vladimir; Tabenkin, Benjamin  
 PA Hoffmann-la Roche Inc.  
 SO U.S., 9 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 3361742	A	19680102	US 1964-416599	19641207
	FR 1553664	A	19690117	FR 1965-1553664	19651203
	BE 673376	A	19660401	BE 1965-673376	19651207
	NL 6515880	A	19660608	NL 1965-15880	19651207
	CH 475997	A	19690731	CH 1965-475997	19651207
	SE 316136	B	19691020	SE 1965-15830	19651207
	BR 6575537	A0	19730906	BR 1965-175537	19651207
PRAI	US 1964-416599	A	19641207		

GI For diagram(s), see printed CA Issue.

AB The title compds., having antibacterial and anticancer activity are produced by culturing *Streptomyces refuineus* var *thermotolerans*, NRRL 3143 or 3144. Extn., purification, and crystn. yields 5,10,11,11a-tetrahydro-9-hydroxy- 11 - methoxy - 8 - methyl - 5 - oxo - 1H - pyrrolo 2,1-c] 1,4]benzodiazepin-2-acrylamide (I). X is 0-1.5. I, when heated with a nonalc. inert solvent (Me2SO, MeCN, Me2CO) at 50.degree.-200.degree. yields II. II, when treated with H2O, yields III. III, when treated with an alc. (Me, Et, Bu, benzyl, .beta.-aminoethyl alc.), a sugar (mannitol), or ethylene glycol, yields IV. Thus, several loopfuls of spores of *Streptomyces* species NRRL 3143 were transferred from a mature (2-3-day-old) 45.degree. stock agar slant to 100 ml. of medium contg. Bacto tryptone 5, Bacto yeast ext. 2, Bacto soytone 2, sol. starch 10, and mannitol 5 g., MgSO4.H2O 200, Fe(NH4)2(SO4)2.6H2O 10, MnCl2.4H2O 1.8, ZnCl2 2.1, CuSO4 H2O 0.3, Co(NO3)2.6H2O 0.5, and H3BO3 0.6 mg./l. in a 1-l. Blake bottle. The medium was incubated at 45.degree. on a rotary shaker for 16 hrs. The contents of 2 Blake bottles were pooled into a 500-ml. transfer bottle fitted with a tubulature at the bottom and contg. 150 ml. of sterile water. The contents were transferred to a 100-gal. stainless steel fermentor prepd. as follows: to 25 gal. of tap water in the fermentor were added potato starch 1500, enzyme-hydrolyzed casein 750, enzyme-hydrolyzed soy protein 300, aq. ext. of yeast 300, mannitol 750, MgSO4.7H2O 30, Fe(NH4)2(SO4)2.6H2O 1.5, and Dow Corning Silicone A emulsion 2.5 g., MnCl2.4H2O 270, ZnCl2 315, CuSO4.5H2O 45, Co(NO3)2.6H2O 75, H3BO3 90 mg. When all the ingredients were dissolved, the vol. was brought to 40 gal. with tap water and the pH adjusted to 7.2 with 60 ml. of 5N KOH. The medium was sterilized by heating to and holding at 120.degree. for 30-40 min. The batch was cooled and inoculated as above. Aeration with 3 cu. ft. of air/min., agitation at a shaft speed of 400 rpm., and a temp. of 48.degree. were used. Sterile 2.5% suspension of Dow Silicone Emulsion AF for control of foam was added as needed. Hourly samples were taken from the 12th hr. on and assayed for in vitro potency. The batch reached its max. potency in 18-20 hrs. The above process was repeated 10 times. The broths were combined, the pH adjusted to 6, and the broth was filtered. The filtrate was extd. countercurrently at 128 gal./hr. with the same rate of BuOH in a Karr extn. column. A water

backwash of 0.2 times the BuOH rate was used at the top of the column to minimize the carryover of water-sol. components. The BuOH ext. was concd. to .apprx.a 5% soln. which was the feed to a Karr fractional liquid extn. column. The column was operated at a H<sub>2</sub>O-BuOH ratio of 10:1 and the BuOH ext. contained the product; the ext. was concd. to a soln. or paste contg. 5-20% solids; 25-50 vols. of n-C<sub>6</sub>H<sub>14</sub> was added and the resulting slurry filtered. The pptd. product was vacuum-dried.

IT **14435-72-4P**

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP  
(Preparation)  
(manuf. of)

RN 14435-72-4 CAPLUS

CN 2-Propenamide, 3-(5,10,11,11a-tetrahydro-9-hydroxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)- (9CI) (CA INDEX NAME)

